```
FILE 'HOME' ENTERED AT 07:37:32 ON 15 NOV 2005
=> file .nash
=> s chronic obstructive lung disease
L1         2293 FILE MEDLINE
L2          361 FILE CAPLUS
L3         1223 FILE SCISEARCH
L4           96 FILE LIFESCI
L5         2236 FILE BIOSIS
L6        23817 FILE EMBASE

TOTAL FOR ALL FILES
L7        30026 CHRONIC OBSTRUCTIVE LUNG DISEASE

=> s l7 and (kunitz or protease inhibitor or proteinase inhibitor)
TOTAL FOR ALL FILES
L14         330 L7 AND (KUNITZ OR PROTEASE INHIBITOR OR PROTEINASE INHIBITOR)

=> s l7 and kunitz
TOTAL FOR ALL FILES
L21           0 L7 AND KUNITZ

=> s l14 and treatment
TOTAL FOR ALL FILES
L28          78 L14 AND TREATMENT

=> s l14 not 1999-2005/py
L36          21 FILE MEDLINE
L37           9 FILE CAPLUS
L38           8 FILE SCISEARCH
L39           1 FILE LIFESCI
L40          23 FILE BIOSIS
L41         109 FILE EMBASE

TOTAL FOR ALL FILES
L42         171 L14 NOT 1999-2005/PY

=> dup rem l42
PROCESSING COMPLETED FOR L42
L43         128 DUP REM L42 (43 DUPLICATES REMOVED)

=> d ibib abs 1-128

L43  ANSWER 1 OF 128  EMBASE  COPYRIGHT (c) 2005 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:   1999008642  EMBASE  Full-text
TITLE:              Proteolytic enzymes and airway diseases.
AUTHOR:             Nadel J.A.; Stockley R.A.
CORPORATE SOURCE:   J.A. Nadel, University of California, Cardiovasc Research
                    Institute, Box 0130, 505 Parnassus Avenue., San Francisco,
                    CA 95143-0130, United States
SOURCE:             European Respiratory Journal, (1998) Vol. 12, No. 6, pp.
                    1250-1251.
                    Refs: 4
                    ISSN: 0903-1936  CODEN: ERJOEI
COUNTRY:            Denmark
DOCUMENT TYPE:      Journal; Editorial
FILE SEGMENT:       015     Chest Diseases, Thoracic Surgery and Tuberculosis
                    029     Clinical Biochemistry
LANGUAGE:           English
ENTRY DATE:         Entered STN: 19990128
                    Last Updated on STN: 19990128
       DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43  ANSWER 2 OF 128  EMBASE  COPYRIGHT (c) 2005 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:   1998406515  EMBASE  Full-text
TITLE:              Neutrophil serine proteinases and defensins in chronic
                    obstructive pulmonary disease: Effects on pulmonary
                    epithelium.
AUTHOR:             Hiemstra P.S.; Van Wetering S.; Stolk J.
```

CORPORATE SOURCE: P.S. Hiemstra, Dept of Pulmonology, Building 1, Leiden University Hospital, P.O. Box 9600, 2300 RC Leiden, Netherlands
SOURCE: European Respiratory Journal, (1998) Vol. 12, No. 5, pp. 1200-1208.
Refs: 103
ISSN: 0903-1936 CODEN: ERJOEI
COUNTRY: Denmark
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990110
Last Updated on STN: 19990110

AB Neutrophils have the capacity to accumulate in high numbers in the lung during infection and inflammation. Because they play an important role in host defence against infection, but may also cause tissue injury, these cells are thought to be involved in the pathogenesis of various inflammatory lung disorders, including chronic bronchitis and chronic obstructive pulmonary disease. Neutrophil products that may mediate tissue injury at sites of neutrophil-dominated inflammation include the neutrophil serine proteinases elastase, cathepsin G and proteinase 3, and the nonenzymatic defensins. One of the targets of the neutrophil is the lung epithelium, and in vitro studies have revealed that both the serine proteinases and neutrophil defensins markedly affect the integrity of the epithelial layer, decrease the frequency of ciliary beat, increase the secretion of mucus, and induce the synthesis of epithelium-derived mediators that may influence the amplification and resolution of neutrophil-dominated inflammation. Both neutrophil elastase and defensins induce the release of the neutrophil chemoattractant chemokine interleukin-8 from respiratory epithelial cells. The α1- proteinase inhibitor (α1-PI) is a well-characterized inhibitor of neutrophil elastase, that also blocks the cytotoxic and stimulatory activity of defensins towards epithelial cells. The elastase inhibitory activity of α1-PI is also abrogated by the binding of defensins to this inhibitor. Incubation of epithelial cells with neutrophil defensins in combination with either elastase or cathepsin G resulted in decreased effects on the epithelial cells compared with those observed when the cells were incubated with defensins, elastase or cathepsin G separately. These results suggest that neutrophil defensins and serine proteinases cause injury and stimulate epithelial cells to produce chemokines that attract more neutrophils to the site of inflammation. The effects of neutrophil defensins and serine proteinases on epithelial cells appear to be restricted by proteinase inhibitors and by inhibitory interactions between these sets of neutrophil granule proteins.

L43 ANSWER 3 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1998331989 EMBASE Full-text
TITLE: Stimulation of the adherence of Haemophilus influenzae to human lung epithelial cells by antimicrobial neutrophil defensins.
AUTHOR: Gorter A.D.; Eijk P.P.; Van Wetering S.; Hiemstra P.S.; Dankert J.; Van Alphen L.
CORPORATE SOURCE: A.D. Gorter, Laboratory for Vaccine Research, Natl. Inst. for Public Health/Envt., P.O. Box 1, NL-3720 BA Bilthoven, Netherlands. Annelies.Gorter@RIVM.NL
SOURCE: Journal of Infectious Diseases, (1998) Vol. 178, No. 4, pp. 1067-1074.
Refs: 37
ISSN: 0022-1899 CODEN: JIDIAQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19981028
Last Updated on STN: 19981028

AB Patients with chronic obstructive pulmonary disease (COPD) frequently have recurrent lower respiratory tract infections with nonencapsulated Haemophilus influenzae. The infected mucosa of these patients is infiltrated with neutrophils, which upon activation may release antimicrobial peptides, including defensins. It was shown that defensins isolated

from neutrophils or from sputum samples of COPD patients did not kill H. influenzae from these patients, but they did stimulate its adherence to human bronchial epithelial cells in a time- and dose-dependent manner. Maximal stimulation was observed after 3 h in the presence of ≤10 μg/mL defensins, resulting in 65 ± 36 cfu/cell (61-fold increase). The enhanced adherence was not solely due to charge effects and was specifically blocked by α1-proteinase inhibitor. Because adherence is the first step in the onset of respiratory tract infections, our findings indicate that neutrophil defensins likely contribute to the pathogenesis of H. influenzae infection in the lower respiratory tract.

L43 ANSWER 4 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998394018 EMBASE Full-text
TITLE: COPD: New developments and therapeutic opportunities.
AUTHOR: Norman P.
CORPORATE SOURCE: Dr. P. Norman, 18 Pink Lane, Burnham, Buckinghamshire SL1 8JW, United Kingdom
SOURCE: Drug News and Perspectives, (1998) Vol. 11, No. 7, pp. 431-437.
ISSN: 0214-0934 CODEN: DNPEED
COUNTRY: Spain
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
014 Radiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990110
Last Updated on STN: 19990110

AB The deficiencies of current therapies and the potential benefits of novel approaches to chronic obstructive pulmonary disease (COPD) were reviewed at a symposium organized at the National Heart and Lung Institute, London, U.K., July 7-8, 1999. Several speakers discussed different facets of the disease. The keynote lecture dealt with two major, but distinct themes: the utility of computerized tomographic scanning as both a quantitative and a qualitative tool and the recent observation that retinoic acid could produce new alveolar growth, emanating from ducts, in hamsters when it was administered after instillation of elastase. Regarding current therapeutic approaches, bronchodilators are the mainstay of existing therapy, while the use of mucolytics varies markedly between countries. The role of steroids in the treatment of COPD is confused. There is surprisingly little evidence of any clinical benefit from the use of antibiotics. Potential future therapies include M3-selective muscarinic antagonists, chemotactic mediators, protease inhibitors and antiinflammatory agents.

L43 ANSWER 5 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998382088 EMBASE Full-text
TITLE: Chronic obstructive pulmonary disease: New opportunities for drug development.
AUTHOR: Barnes P.J.
CORPORATE SOURCE: Prof. P.J. Barnes, National Heart and Lung Institute, Imperial College School of Medicine, Dovehouse Street, London SW3 6LY, United Kingdom
SOURCE: Trends in Pharmacological Sciences, (1998) Vol. 19, No. 10, pp. 415-423.
Refs: 78
ISSN: 0165-6147 CODEN: TPHSDY
PUBLISHER IDENT.: S 0165-6147(98)01245-0
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990122
Last Updated on STN: 19990122

AB Chronic obstructive pulmonary disease (COPD) is common and there is an increasing worldwide prevalence. There are no available treatments to prevent the progression of

airflow obstruction, but greater understanding of the molecular and cellular mechanisms involved in COPD has identified many new therapeutic targets, including inflammatory mediators, proteases and adhesion molecules. In this review, Peter Barnes considers potential new drugs for this neglected disease. Copyright (C) 1998 Elsevier Science Ltd.

L43 ANSWER 6 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998166323 EMBASE Full-text
TITLE: Management of COPD: Early identification and active intervention are crucial.
AUTHOR: Ferguson G.T.
CORPORATE SOURCE: Dr. G.T. Ferguson, Harper Hospital-3 Hudson, 3990 John R, Detroit, MI 48025, United States. gferguson@oncgate.roc.wayne.edu
SOURCE: Postgraduate Medicine, (1998) Vol. 103, No. 4, pp. 129-141.
Refs: 34
ISSN: 0032-5481 CODEN: POMDAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19980618
Last Updated on STN: 19980618

AB Medical management of COPD begins with an awareness of risk factors and identification of at-risk patients. Once disease is identified, patient and family education, a smoking cessation program, and an appropriate bronchodilator regimen should be initiated. Airway secretions and infections should be minimized, hypoxemia corrected, and other secondary physiologic disturbances evaluated when appropriate. Participation in a comprehensive pulmonary rehabilitation program can markedly improve symptoms, function, exercise performance, and quality of life. The results are a reduction in patient limitations, medical expenses, and dependence on medical facilities and caregivers.

L43 ANSWER 7 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998089448 EMBASE Full-text
TITLE: Strategies in preserving lung health and preventing COPD and associated diseases: The National Lung Health Education Program (NLHEP).
AUTHOR: Bailey W.C.; Ferguson G.T.; Higgins M.; Hudson L.D.; Miller R.D.; Masferrer R.; Nair S.; Rennard S.I.; Petty T.L.; Shure D.; Hindi-Alexander M.; Weinmann G.; Hurd S.S.
SOURCE: Chest, (1998) Vol. 113, No. 2 SUPPL., pp. 123S-163S.
Refs: 156
ISSN: 0012-3692 CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
017 Public Health, Social Medicine and Epidemiology
036 Health Policy, Economics and Management
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 19980409
Last Updated on STN: 19980409
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 8 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998253728 EMBASE Full-text
TITLE: [Role of nebulization in chronic obstructive pulmonary disease].
PLACE DE LA NEBULISATION DANS LES BRONCHOPNEUMOPATHIES CHRONIQUES OBSTRUCTIVES.
AUTHOR: Huchon G.
CORPORATE SOURCE: G. Huchon, Service de Pneumologie, Hopital Ambroise Pare, Boulogne-Billancourt, France
SOURCE: Revue de Pneumologie Clinique, (1998) Vol. 54, No. SUPPL.

1, pp. S26-S27.
Refs: 4
ISSN: 0032-5821 CODEN: RPCLEZ
COUNTRY: France
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: French
ENTRY DATE: Entered STN: 19980820
Last Updated on STN: 19980820
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 9 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 97103289 EMBASE Full-text
DOCUMENT NUMBER: 1997103289
TITLE: Biosynthesis of α1-proteinase inhibitor by human lung-derived epithelial cells.
AUTHOR: Cichy J.; Potempa J.; Travis J.
CORPORATE SOURCE: J. Travis, Biochemistry/Molecular Biology Dept., University of Georgia, Athens, GA 30602, United States
SOURCE: Journal of Biological Chemistry, (1997) Vol. 272, No. 13, pp. 8250-8255.
Refs: 23
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 970429
Last Updated on STN: 970429
AB Destruction of components of the extracellular matrix of the lung by neutrophil elastase is believed to be a critical event in the development of obstructive lung disease. The local synthesis of α1- proteinase inhibitor, the controlling inhibitor of this enzyme, may provide a partial mechanism for neutrophil elastase regulation, especially during inflammation, when proteolytic enzymes are released from phagocytes. In this study, we show that lung-derived epithelial cells not only have the capacity to synthesize functional α1-PI but also to increase the rate of its production when stimulated by specific inflammatory mediators, including oncostatin M, interleukin-1, and the glucocorticoid analogue, dexamethasone.

L43 ANSWER 10 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 97245660 EMBASE Full-text
DOCUMENT NUMBER: 1997245660
TITLE: PI SZ phenotype in chronic obstructive pulmonary disease.
AUTHOR: Alvarez-Granda L.; Cabero-Perez M.J.; Bustamante-Ruiz A.; Gonzalez-Lamuno D.; Delgado-Rodriguez M.; Garcia-Fuentes M.
CORPORATE SOURCE: Dr. M. Garcia-Fuentes, Department of Paediatrics, University Hospital of Valdecilla, Santander, Spain
SOURCE: Thorax, (1997) Vol. 52, No. 7, pp. 659-661.
Refs: 11
ISSN: 0040-6376 CODEN: THORA7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
007 Pediatrics and Pediatric Surgery
015 Chest Diseases, Thoracic Surgery and Tuberculosis
017 Public Health, Social Medicine and Epidemiology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 970904
Last Updated on STN: 970904
AB Background - A study was undertaken to clarify whether the Pi SZ phenotype of the protease inhibitor system predisposes to chronic obstructive pulmonary disease (COPD). Methods - The prevalence of PI Z and PI SZ deficient phenotypes was investigated in a population of

702 patients with COPD followed up at the Chest Unit of a tertiary hospital and in 15 400 newborn infants from the same geographical area. Individuals with deficiency were detected by screening of dried blood spots on filter paper using a comparative electroimmunodiffusion technique for α1-anti-trypsin and transferrin. The serum phenotype was confirmed by means of isoelectrofocusing on polyacrylamide gel. Results - Of the 702 blood samples from patients with COPD, six PI Z subjects (0.85%) and one PI SZ (0.14%) were detected. Of the 15 400 samples from neonates, the number of PI Z subjects was eight (0.052%) and that of PI SZ was 24 (0.156%). The difference between the two groups was significant for PI Z but not for PI SZ. Conclusions - The data do not indicate an increased risk for development of COPD associated with the PI SZ phenotype but confirm the predisposition of PI Z individuals for the development of COPD.

L43 ANSWER 11 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998041916 EMBASE Full-text
TITLE: Chronic obstructive pulmonary disease from science to the clinic: The role of glutathione in oxidant-antioxidant balance.
AUTHOR: MacNee W.
CORPORATE SOURCE: W. MacNee, Respiratory Medicine Unit, Dept. of Medicine, Royal Infirmary, Edinburgh EH3 9YW, United Kingdom
SOURCE: Monaldi Archives for Chest Disease, (1997) Vol. 52, No. 5, pp. 479-485.
Refs: 49
ISSN: 1122-0643 CODEN: MACDEL
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 19980220
Last Updated on STN: 19980220
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 12 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998025654 EMBASE Full-text
TITLE: α1-antitrypsin deficiency: Memorandum from a WHO meeting.
AUTHOR: Barker A.; Brantly M.; Campbell E.; Carrell R.; Cox D.W.; Dirksen A.; Dodge J.A.; El-Hazmi M.A.F.; Eriksson S.; Ginter E.K.; McElvaney N.G.; Mehta A.; Propst A.; Sandhaus R.; Snider G.L.; Stockley R.A.; Stoller J.K.; Verma I.C.; Walsh J.; Wencker M.; Napalkov N.P.; Tsechkovski M.; Boulyjenkov V.; Heuck C.-C.
CORPORATE SOURCE: Dr. V. Boulyjenkov, Human Genetics Programme, World Health Organization, 1211 Geneva 27, Switzerland
SOURCE: Bulletin of the World Health Organization, (1997) Vol. 75, No. 5, pp. 397-415.
Refs: 81
ISSN: 0042-9686 CODEN: BWHOA6
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
017 Public Health, Social Medicine and Epidemiology
022 Human Genetics
029 Clinical Biochemistry
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 19980205
Last Updated on STN: 19980205

AB α1-Antitrypsin (AAT) deficiency, also known as α1-antiprotease inhibitor deficiency, is a disease caused by genetically determined AAT deficiency. It occurs as a result of inheritance of two protease inhibitor (PI) deficiency alleles from the AAT gene locus (designated PI) on chromosomal segment 14q32.1. The most common deficiency allele is PI*Z

and a large majority of individuals with severe AAT deficiency are PI type ZZ. The disease occurs predominantly in white persons of European origin and its frequency in Europe and North America is comparable to that of cystic fibrosis (1 in 2000 to 1 in 7000.) Persons with AAT deficiency may have no clinical manifestations. Chronic obstructive pulmonary disease (COPD) with a high frequency of panacinar emphysema is the most prevalent clinical disorder associated with AAT deficiency and the most frequent cause of disability and death. Tobacco smoking is the major risk factor for developing COPD, which generally begins by the third decade of life, much earlier than 'usual' COPD that occurs in AAT-replete individuals. Liver disease, the second most frequent clinical manifestation of AAT deficiency, typically presents as cholestasis in infancy but is usually not severe and generally remits by adolescence. Chronic liver disease develops infrequently, although AAT deficiency is the commonest cause of chronic liver disease in childhood. Cirrhosis and carcinoma of the liver affect at least 25% of AAT-deficient adults over the age of 50 years. AAT deficiency appears to be widely underdiagnosed and based on predicted gene frequencies even in the most intensely studied populations, only a small proportion of those predicted to have AAT deficiency have been diagnosed. Human AAT is available in limited quantity for augmentation therapy. This Memorandum summarizes the discussions and recommendations made by participants at a WHO meeting held in Geneva on 18-20 March 1996 to review existing knowledge about this highly prevalent genetic disorder, develop a strategy for enhancing awareness of it among health-care-givers and the general public, and explore new case-finding and disease-prevention strategies.

L43 ANSWER 13 OF 128 EMBASE

ACCESSION NUMBER: 97187107 EMBASE Full-text
DOCUMENT NUMBER: 1997187107
TITLE: [Latest information on the pathogenesis of obstructive airway diseases influencing their legal assessment as an occupational disease].
DER EINFLUSS NEUER ERKENNTNISSE ZUR PATHOGENESE OBSTRUKTIVER ATEMWEGSERKRANKUNGEN UND IHRE BK-RECHTLICHE BEWERTUNG.
AUTHOR: Matthys H.; Virchow J.C.; Kroegel C.
CORPORATE SOURCE: Prof. Dr. H. Matthys, Klinikum, Albert-Ludwig-Universitat, Abteilung Pneumologie, Hugstetter Strasse 55, D-79106 Freiburg, Germany
SOURCE: Zentralblatt fur Arbeitsmedizin, Arbeitsschutz und Ergonomie, (1997) Vol. 47, No. 5, pp. 172-177.
Refs: 27
ISSN: 0944-2502 CODEN: ZAAEEL
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
035 Occupational Health and Industrial Medicine
LANGUAGE: German
SUMMARY LANGUAGE: English; German; French
ENTRY DATE: Entered STN: 970731
Last Updated on STN: 970731

AB Today the term exogenic-allergic asthma with eosinophilic inflammation, specific IgE antibodies is the best-defined condition of the group of obstructive airway diseases for the BKV. Since genetic factors predispose for that kind of disease, the surroundings at work can at best induce or enhance it. Such patients have to be protected against inhalative allergenic and unspecific stimuli (chemical, irritative) in an appropriate way or excluded from occupational stress factors. There are little (Isocyanate, aspirin) 'specific' exogenic inductors for intrinsic asthma: professional exposure can therefore rarely be the cause (preventive vocational guidance). The most frequent cause for chronic obstructive bronchitis is tobacco smoke, a fact that can mask all other causes and lead to complications. Chemically and physically irritative additions to the air will lead from an acute to a chronic, regenerative, non-eosinophilic inflammation which - unlike asthma - involves a carcinogenic and emphysematous risk. The term 'asthma' should not be used in this context. Model exposures and MAK-values should provide the necessary aetiologic-diagnostic and industrial safety concentrations. Short-term exposures to pollutants mostly lead to combined - mainly restrictive - and slight, obstructive ventilatory disorders (from acute gas pulmonary oedema to isocyanate, quartz and asbestos exposure and exogenic-allergic aerosols with or without precipitating antibody formation). Chronically low gas and aerosol exposure (NO(x), SO2, byssinosis, mixed dust pneumoconiosis) leads to chronic bronchitis with more or less centrilobular emphysema. The inhalation patterns can cause a bronchial hyperreaction or enhance an already existing one. The variability of this

hyperreactivity is lower and less distinct than for exogenic-allergic asthma. Unlike an asthmatic inflammation, metaplasia, hyperplasia and dysplasia can result in a carcinoma in situ (syncarcinogenesis, uranium dust, asbestos and quartz dust etc.). Due to a lack of a proteinase inhibitor in the serum, the predisposition for an emphysema is only predictable for an infinitely small number of patients. If a lack of α1-PI is detected (≤30% standard), the patient should be dispensed from any inhalative stress. If there is a loss of FEV1 > 120 ml/year, the α1-PI deficiency should be substituted. Today, a bronchoscopic examination of the lung (BAL, biopsy of the mucosa, transbronchial biopsy, segmental provocation, if necessary) should be the diagnostic aim and is reasonable as to the risks, if anamnesis, data on pulmonary function and exposure indicate an occupational disease. CT scans and X-rays are often overinterpreted to find the cause of occupational lung damages.

L43 ANSWER 14 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 97261595 EMBASE Full-text
DOCUMENT NUMBER: 1997261595
TITLE: Oxidative stress in COPD.
AUTHOR: Jorres R.A.; Magnussen H.
CORPORATE SOURCE: R.A. Jorres, Krankenhaus Grosshansdorf, Zentrum Pneumologie Thoraxchirurgie, LVA Freie und Hansestadt Hamburg, Wohrendamm 80, D-22929 Grosshansdorf, Germany
SOURCE: European Respiratory Review, (1997) Vol. 7, No. 43, pp. 131-135.
Refs: 34
ISSN: 0905-9180 CODEN: EREWEH
COUNTRY: Denmark
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 970918
Last Updated on STN: 970918

AB There is strong evidence that reactive oxygen species (ROS) play a major role in the development of emphysema and chronic obstructive pulmonary disease (COPD). This is particularly true in view of cigarette smoking as the most important determinant in these diseases. Reactive compounds contained in cigarette smoke exert exogenous oxidative stress, which is enhanced and possibly superseded by endogenous oxidative stress arising from the generation of ROS by inflammatory cells present in increased numbers or activated form within the airways. The effects of ROS comprise lipid peroxidation and oxidative protein damage, which reduces or abolishes the biological activity of receptors or antiproteases and leads to direct or indirect destruction of lung tissue. It remains to be determined whether interindividual differences in antioxidant capacity contribute to the differences in the susceptibility against cigarette-smoke induced CORD.

L43 ANSWER 15 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 96118379 EMBASE Full-text
DOCUMENT NUMBER: 1996118379
TITLE: Aerosolized human neutrophil elastase induces airway constriction and hyperresponsiveness with protection by intravenous pretreatment with half- length secretory leukoprotease inhibitor.
AUTHOR: Suzuki T.; Wang W.; Lin J.-T.; Shirato K.; Mitsuhashi H.; Inoue H.
CORPORATE SOURCE: Third Dept. of Internal Medicine, Iwate Medical Univ. Sch. of Medicine, 19-1 Uchimaru,Morioka 020, Japan
SOURCE: American Journal of Respiratory and Critical Care Medicine, (1996) Vol. 153, No. 4, pp. 1405-1411.
ISSN: 1073-449X CODEN: AJCMED
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 960507

Last Updated on STN: 960507

AB This study was designed to determine the effects of inhaled human neutrophil elastase (HNE) on airway constriction and airway responsiveness, and to examine the protection by an intravenous recombinant half-length secretory leukoprotease inhibitor, r1/2SLPI in guinea pigs. Aerosol inhalation of HNE (250 μg/ml, for 3 min) caused a transient but significant airway constriction, in which lung resistance (RL) increased from 194 ± 18 (mean ± SEM) to 461 ± 42 cm H2O/L/s ($p < 0.001$). Thirty minutes after the end of HNE inhalation, airway responsiveness to intravenous 5- hydroxytryptamine (5-HT) was significantly increased. The provocative dose causing a 200% increase in RL (PD200) was significantly decreased from 10.0 ± 1.2 to 6.5 ± 0.8 μg/kg ($p < 0.001$). Forty-five minutes after the end of HNE inhalation, total cells in bronchoalveolar lavage fluid (BALF) were significantly increased ($p < 0.05$). Histologic study of intrapulmonary bronchi demonstrated an acute inflammatory response characterized by damage to the epithelium, airway obstruction by mucus plugs, and recruitment of mononuclear and polymorphonuclear cells to the bronchial epithelium. r1/2SLPI (30 mg/kg) injected 5 min before the initiation of HNE inhalation significantly inhibited the airway constriction ($p < 0.05$), the airway hyperresponsiveness ($p < 0.01$), and the increase of cells in BALF ($p < 0.05$). The present data suggest that HNE plays a role in the induction of airway constriction and airway hyperresponsiveness in various inflammatory lung diseases with pulmonary neutrophil infiltration, such as chronic obstructive pulmonary diseases (COPD) and possibly bronchial asthma. r1/2SLPI may be useful as an antiprotease treatment.

L43 ANSWER 16 OF 128 EMBASE

ACCESSION NUMBER: 96356398 EMBASE Full-text
DOCUMENT NUMBER: 1996356398
TITLE: Cystic fibrosis.
AUTHOR: Davis P.B.; Drumm M.; Konstan M.W.
CORPORATE SOURCE: Case Western Reserve University, 2109 Adelbert Rd.,Cleveland, OH 44106-4948, United States
SOURCE: American Journal of Respiratory and Critical Care Medicine, (1996) Vol. 154, No. 5, pp. 1229-1256.
ISSN: 1073-449X CODEN: AJCMED
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 961218
Last Updated on STN: 961218

AB Investigators in CF can study at the molecular level a disease in which a single-gene defect gives rise to a variety of pathophysiologic disorders in many organ systems, most notably the lung. Despite the enormous recent progress in CF research, unanswered questions remain, some of which are highly relevant to the de sign of new therapies, especially those directed at the basic defect. Of particular importance is discovering how the defect in CFTR gives rise to infection and inflammation in the CF lung. Widespread acceptance of aggressive treatment programs at Centers around the country has increased median survival for patients with CF nationwide to 29 yr. However, the symptomatic therapies that have brought the patients this far, even if they can be refined, will probably not take us much farther. The CFF Data Registry reports that survival of patients with CF has not increased in 5 yr (9). New strategies of treatment will be necessary to improve survival further. One such new strategy may be wider application of anti-inflammatory therapy, which was reported only last year to slow the rate of pulmonary decline in young, relatively healthy patients with CF (318). There has not been time to see the impact of anti-inflammatory therapy on survival, and it will probably take several years. However, even this is a rear guard action, addressing a consequence of CF and not a cause. There is hope that the understanding of the underlying pathophysiology of CF will allow us to attack the disease at its root, possibly by manipulation of epithelial ion transport, or by activation of mutant protein, or by provision of the normal gene for CFTR to the appropriate cells. These therapies are in various stages of development, and they have raised important basic questions that must now be answered before further progress can occur. CF is a striking example of the bench to bedside continuum of research.

L43 ANSWER 17 OF 128 EMBASE

ACCESSION NUMBER: 96303768 EMBASE Full-text
DOCUMENT NUMBER: 1996303768
TITLE: Role of oxidants/antioxidants in smoking-induced lung diseases.
AUTHOR: Rahman I.; MacNee W.
CORPORATE SOURCE: Unit of Respiratory Medicine, Department of Medicine, Royal Infirmary, Lauriston Place,Edinburgh EH3 9YW, United Kingdom
SOURCE: Free Radical Biology and Medicine, (1996) Vol. 21, No. 5, pp. 669-681.
ISSN: 0891-5849 CODEN: FRBMEH
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 961028
Last Updated on STN: 961028

AB An imbalance between oxidants and antioxidants has been considered in the pathogenesis of smoking-induced lung diseases, such as chronic obstructive pulmonary disease (COPD), particularly emphysema. Recent evidence indicates that increased neutrophil sequestration and activation occurs in the pulmonary microvasculature in smokers and in patients with COPD, with the potential to release reactive oxygen species (ROS). ROS generated by airspace phagocytes or inhaled directly from the environment also increase the oxidant burden and may contribute to the epithelial damage. Although much research has focused on the protease/antiprotease theory of the pathogenesis of emphysema, less attention has been paid to the role of ROS in this condition. The injurious effects of the increased oxidant burden in smokers and in patients with COPD are opposed by the lung antioxidant defences. Hence, determining the mechanisms regulating the antioxidant responses is critical to our understanding of the role of oxidants in the pathogenesis of smoking- induced lung diseases and to devising future strategies for antioxidant therapy. In this article we have reviewed the evidence for the presence of an oxidant/antioxidant imbalance in smoking-induced lung disease and its relevance to therapy in these conditions.

L43 ANSWER 18 OF 128 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:333971 CAPLUS Full-text
DOCUMENT NUMBER: 125:31226
TITLE: Inhibition of the protease activity in tracheobronchial aspirates of horses with chronic obstructive pulmonary disease
AUTHOR(S): Koivunen, Anna-Liisa; Maisi, Paivi; Fang, Weihuan; Sandholm, Markus
CORPORATE SOURCE: Faculty of Veterinary Medicine, University of Helsinki, Helsinki, FIN-00014, Finland
SOURCE: American Journal of Veterinary Research (1996), 57(5), 603-607
CODEN: AJVRAH; ISSN: 0002-9645
PUBLISHER: American Veterinary Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to clarify the role of proteolytic enzymes in the pathogenesis of chronic obstructive pulmonary disease (COPD) in horses, and to investigate new possibilities for treatment of this disease by interfering in the proteolytic process. The effect of antiproteolytic activity of selected **protease inhibitors** on tracheal aspirates was studied in vitro, and the inhibition profiles were compared with those of purified proteases. Respiratory tract secretions with antiproteolytic activity from 9 horses with COPD were studied using the caseinolytic-diffusion assay. The protease-inhibition profile of tracheal aspirates differed from horse to horse. The profiles did not resemble that of any of the pure proteases. Acetylcysteine, pentamidine, and diminazene were most effective in inhibiting proteolytic activity in tracheal aspirates in vitro. The authors concluded that a mixed type of proteolytic activity is present in the respiratory tract secretions of horses with COPD. Acetylcysteine, pentamidine, and diminazene seem to have potential to be used in vivo to protect the lungs of horses with COPD from proteolytic damage.

reserved on STN
ACCESSION NUMBER: 97041732 EMBASE Full-text
DOCUMENT NUMBER: 1997041732
TITLE: Cellular mechanisms in the pathogenesis of COPD.
AUTHOR: Stockley R.A.
CORPORATE SOURCE: R.A. Stockley, Lung Investigation Unit, Nuffield House, The Queen Elizabeth Hospital, Birmingham B15 2TH, United Kingdom
SOURCE: European Respiratory Review, (1996) Vol. 6, No. 39, pp. 264-269.
Refs: 30
ISSN: 0905-9180 CODEN: EREWEH
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 970224
Last Updated on STN: 970224

AB Studies have indicated that proteolytic enzymes, including neutrophil elastase, may result in pathological changes similar to human emphysema and chronic bronchitis when instilled into the airways of animals. Furthermore, a deficiency in α1-antitrypsin, the inhibitor for neutrophil elastase, has been associated with the early onset of chronic bronchitis and emphysema, since this deficiency causes a reduction in the antiproteinase screen protecting the lung tissue. This observation has led to the concept that chronic obstructive pulmonary disease (COPD) is related to an imbalance between proteinases and antiproteinases. However, since many patients with COPD do not have low levels of α1-antitrypsin, it is presently unclear what role this factor plays in the development of the disease. An influx of neutrophils into the lung occurs in response to chemoattractants, such as interleukin-8, in patients with COPD. This increased chemotactic response results in increased degranulation and, therefore, greater lung tissue destruction. It is, therefore, possible that the processes of inflammatory cell migration and activation play a key role in the development of lung damage typical of the pathology of COPD. Potential therapies may be designed to interrupt specific steps in the migration and degranulation of neutrophils. Therefore, lung tissue destruction by proteolytic enzymes might be reduced by supplementing levels of antiproteinase inhibitor, thereby enhancing the protective antiproteinase screen within the lung. Since cell recruitment and activation are thought to be key factors in the pathogenesis of COPD, an alternative approach may be to modulate factors that influence this process, for example by downregulation of the chemotactic response and possibly the destructive potential of inflammatory cells.

L43 ANSWER 20 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 96207521 EMBASE Full-text
DOCUMENT NUMBER: 1996207521
TITLE: [Pathogenesis of chronic obstructive pulmonary disease. With emphasis on pulmonary emphysema]. ETIOPATOGENESIS DE LA ENFERMEDAD PULMONAR OBSTRUCTIVA CRONICA. CON ENFASIS EN EL ENFISEMA PULMONAR.
AUTHOR: Sansores R.H.; Ramos Abraham C.; Ramirez-Venegas A.; Mejia-Alfaro R.; Sanchez C.; Montano Ramirez M.
CORPORATE SOURCE: Clinica de EPOC, Inst. Nac. de Enfermedades Resp., Calzada de Tlalpan 4502,Mexico, D.F. 14080, Mexico
SOURCE: Revista del Instituto Nacional de Enfermedades Respiratorias, (1996) Vol. 9, No. 2, pp. 145-154.
ISSN: 0187-7585 CODEN: RNERFG
COUNTRY: Mexico
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: Spanish
SUMMARY LANGUAGE: English; Spanish
ENTRY DATE: Entered STN: 960830
Last Updated on STN: 960830

AB Chronic obstructive pulmonary disease is a term which included chronic bronchitis, small airways disease and pulmonary emphysema. After defining each entity, in this work we focused on the pathogenesis of the airflow obstruction as a single entity, without considering the magnitude in which either emphysema or small airway disease contribute to

such obstruction. Although in general terms the same risk factors are involved in the pathogenesis of the three disorders, the possible mechanisms by which those factors may lead to the airflow limiation are discussed. Finally, concerning to pulmonary emphysema, the hypothesis currently accepted to explain the destructive events observed in the lungs, the protease-antiprotease theory, was comprehensively revised.

L43 ANSWER 21 OF 128 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 96091959 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8525333
TITLE: [Guidelines for the diagnosis and treatment of chronic obstructive lung disease--effective and necessary].
Richtlinien fur die Diagnose und Behandlung der chronischen obstruktiven Lungenkrankheit--wirksam und notwendig.
AUTHOR: Brandli O
CORPORATE SOURCE: Zurcher Hohenklinik Wald, Faltigberg.
SOURCE: Schweizerische medizinische Wochenschrift, (1995 Nov 11) 125 (45) 2164-7.
Journal code: 0404401. ISSN: 0036-7672.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960219
Last Updated on STN: 19960219
Entered Medline: 19960119

AB The independent practice of the art of medicine which doctors took for granted in the past has ended. With almost revolutionary speed, insurers, administrators and politicians have distributed the unique relationship between doctors and their patients. Treatment and diagnostic guidelines in different clinical entities have been based on the pillars of medicine - controlled studies and/or a common consensus among specialists and practitioners. These dynamic activities have enriched our knowledge and practice of medicine. However, only the continuing direct collaboration of physicians at all levels and constant adjustment to changing conditions make these guidelines applicable to the ever changing world of medicine. Chronic obstructive lung disease is one such clinical entity that requires uniform guidelines. Issues that have to be addressed are not only who belongs in this category but also what interventions, such as lateral chest radiographs, CT scans and sleep lab investigations, should be performed as well as the indications for costly therapies such as long-term home oxygen, alpha-1-protease inhibitor augmentation therapy and lung transplantations. Instead of looking at guidelines at straitjackets that limit excellence in the practice of medicine, medical associations should treat them as an opportunity to define their own quality standards. By doing so, the medical community would eliminate the influence of administrative directions or gatekeeper decisions, while patients and the whole population would greatly benefit.

L43 ANSWER 22 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 95364628 EMBASE Full-text
DOCUMENT NUMBER: 1995364628
TITLE: Excessive neutrophil elastase in bronchoalveolar lavage fluid in subclinical emphysema.
AUTHOR: Yoshioka A.; Betsuyaku T.; Nishimura M.; Miyamoto K.; Kondo T.; Kawakami Y.
CORPORATE SOURCE: First Department of Medicine, Hokkaido Univ. School of Medicine, Kita 15, Nishi 7,Kita-ku, Sapporo 060, Japan
SOURCE: American Journal of Respiratory and Critical Care Medicine, (1995) Vol. 152, No. 6 I, pp. 2127-2132.
ISSN: 1073-449X CODEN: AJCMED
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 951228
Last Updated on STN: 951228

AB In an attempt to further evaluate the role of neutrophil elastase (NE) in the development of emphysema, we examined the immunologic quantity of NE bound to α1-protease inhibitor (PI), the NE inhibitory activity, and the molecular pattern of α1-PI in unconcentrated

bronchoalveolar lavage fluid (BALF) supernatant from 36 community-based older volunteers. They were classified into three groups: 10 current smokers with low attenuation areas (LAAs) on the lung computed tomography (CT) scans who were considered to have subclinical emphysema, 13 current smokers who had a comparable smoking history but no LAA, and 13 noncurrent smokers without LAA. The concentration of NE-α1-PI complex was significantly increased in the subjects with subclinical emphysema when compared not only with the noncurrent smokers (0.52 ± 0.10 versus 0.21 ± 0.03 SEM μg/mg albumin, $p < 0.01$) but also with the LAA(-) current smokers (0.52 ± 0.10 versus 0.23 ± 0.07 SEM μg/mg albumin, $p < 0.01$). NE inhibitory activity measured by a spectrophotometric method using methoxysuccinyl-alanyl-alanyl-prolyl-valyl- paranitroanilide did not show any significant difference between the two groups of current smokers. There was no difference in the pattern or density of native and proteolysed α1-PI bands between the three groups by Western blotting. We conclude that NE-α1-PI complex in BALF is a factor that may differentiate smokers who are potentially developing emphysema from those who are not.

L43 ANSWER 23 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 95261888 EMBASE Full-text
DOCUMENT NUMBER: 1995261888
TITLE: [The multiple subject approach to the chronic obstructive pulmonary disease].
ABORDAGEM MULTIDISCIPLINAR DA DOENCA PULMONAR OBSTRUTIVA CRONICA (DPOC).
AUTHOR: Santos Torres B.; Martins Barros A.R.
CORPORATE SOURCE: Av. Jose Bonifacio, 1141,CEP 50710-000-Torre-Recife, Brazil
SOURCE: Revista Brasileira de Medicina, (1995) Vol. 52, No. 7, pp. 705-712.
ISSN: 0034-7264 CODEN: RBMEAU
COUNTRY: Brazil
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: Portuguese
SUMMARY LANGUAGE: Portuguese; English
ENTRY DATE: Entered STN: 951003
Last Updated on STN: 951003

AB Due to the complexity of the treatment of COPD carriers, a multiple subject participation is fundamental, providing an ample approach aiming at the correction of various disturbances which appear during the evolution of the patients. Modern Pharmacological Therapy, through the judicious use of bronchodilators, anti-infectious agents, corticosteroids and anti-protease substitution therapy, has provided major advances in the treatment of this disease, with a consequent substantial improvement of the results. Primordial efforts must be made to control tabaccoism in an attempt to prevent the initiation to the vice. The integration of tobaccoism control actions with those of early diagnosis and treatment, will certainly bring greater benefits preventing or detecting alterations still susceptible to spontaneous regression. The combined effort in the direction of a better hygienic-dietetic orientation, rehabilitation of the pulmonary functional capacity, psychological support for emotional control, and occupational therapy comprise a more dynamic treatment with better chances of giving back to the patient his freedom with a better quality of life, therefore reintegrating him or her to the same society which is inclined to dispose of the person when he or she is no longer able to perform productive activities.

L43 ANSWER 24 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 95057206 EMBASE Full-text
DOCUMENT NUMBER: 1995057206
TITLE: Effect of cigarette smoking on pulmonary function in each phenotype M of α-1-protease inhibitor.
AUTHOR: Matsuse T.; Fukuchi Y.; Matsui H.; Sudo E.; Nagase T.; Orimo H.
CORPORATE SOURCE: Dept. of Geriatrics, University of Tokyo, 7-3-1 Hongo,Bunkyo-ku, Tokyo 113, Japan
SOURCE: Chest, (1995) Vol. 107, No. 2, pp. 395-400.
ISSN: 0012-3692 CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
017 Public Health, Social Medicine and Epidemiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 950308
Last Updated on STN: 950308

AB Human α-1-protease inhibitor (α-1-Pi) has been known to be a highly polymorphic protein. We hypothesized that antiprotease activity of each phenotype M of α1-protease inhibitor (PiM) might be different among smokers and that a variation of decrease in pulmonary function for a given amount of cigarette smoking might be associated with PiM phenotypes. To test this, we investigated the effect of cigarette smoking on pulmonary function in each PiM phenotype. The serum level of α1-Pi was measured by the turbidimetric immunoassay and the distribution of PiM phenotypes was determined using isoelectric focusing technique in 247 healthy subjects and 20 COPD patients. Serum levels of α-1-antitrypsin of healthy and COPD subjects were 205.1 ± 31.1 and 179.2 ± 44.4 (±SD) mg/dL, respectively ($p>0.01$). The frequency of each PiM phenotype in healthy subjects was shown as follows: M1, 0.555; M1M2, 0.328; M2, 0.041; M1M3, 0.057; M2M3, 0.016; M3, 0.004. The difference in the distribution of PiM phenotypes between healthy and COPD subjects was not significant. Single- and multiple-regression analyses showed that the ratio of FEV1 to forced vital capacity (FVC), in which FEV1 is expressed as percentage of FVC, the maximum flow rate at 50% of FVC divided by measured body height (V50/Ht), and the maximum flow rate at 25% of FVC divided by body height (V25/H1) were closely related to age and that V25/Ht also was related to smoking index. However, PiM phenotype was unrelated to those pulmonary function variables. We conclude that PiM phenotype is not a major determinant of difference in magnitude of pulmonary impairments caused by cigarette smoking in each individual.

L43 ANSWER 25 OF 128 EMBASE
ACCESSION NUMBER: 96027119 EMBASE Full-text
DOCUMENT NUMBER: 1996027119
TITLE: Antileucoprotease in the airways and emphysema.
AUTHOR: Dijkman J.H.
CORPORATE SOURCE: Dept. of Pneumology C3-P, Academisch Ziekenhuis, Rijnsburgerweg 10,2300 RC Leiden, Netherlands
SOURCE: Monaldi Archives for Chest Disease, (1995) Vol. 50, No. 5, pp. 383-387.
ISSN: 1122-0643 CODEN: MACDEL
COUNTRY: Italy
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 960206
Last Updated on STN: 960206

AB Antileucoprotease (ALP) is a natural occurring anti-elastase, and is produced in the epithelium of the conducting airways. It is a small protein, consisting of 107 amino-acids arranged in 2 domains. The second domain carries the antiproteolytic active site, the first is responsible for anti-microbial activity. In hamsters, intratracheal installation of ALP prevents the development of emphysema after administration of elastase. The daily production of ALP is remarkably constant, even during exacerbations of COPD. In the human lung a positive correlation was found between the number of ALP-producing bronchiolar cells and small airway's disease and emphysema. ALP is able to penetrate the alveolar-capillary membrane and has a tendency to associate with elastic fibers.

L43 ANSWER 26 OF 128 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 95219430 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7704565
TITLE: The pathogenesis of chronic obstructive lung diseases: implications for therapy.
AUTHOR: Stockley R A
CORPORATE SOURCE: Lung Immunobiochemical Research Laboratory, University of Birmingham, UK.
SOURCE: QJM : monthly journal of the Association of Physicians, (1995 Feb) 88 (2) 141-6. Ref: 39
Journal code: 9438285. ISSN: 1460-2725.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950518
Last Updated on STN: 20000303
Entered Medline: 19950508

L43 ANSWER 27 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 95119933 EMBASE Full-text
DOCUMENT NUMBER: 1995119933
TITLE: The search for susceptibility genes of COPD.
AUTHOR: Luisetti M.; Pignatti P.F.
CORPORATE SOURCE: Ist. Tisiolog. Malattie Respiratorie, Universita degli Studi di Pavia, IRCCS Policlinico San Matteo, via Taramelli 5,27100 Pavia, Italy
SOURCE: Monaldi Archives for Chest Disease, (1995) Vol. 50, No. 1, pp. 28-32.
ISSN: 1122-0643 CODEN: MACDEL
COUNTRY: Italy
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 950503
Last Updated on STN: 950503
AB Environmental factors, such as cigarette smoking, outdoor and indoor pollution, and childhood respiratory infections, are believed to play a major role as risk factors for developing chronic obstructive pulmonary disease (COPD), The only confirmed genetic risk factor for COPD is the inherited deficiency of α1-proteinase inhibitor. However, the evidence of familial clustering of lung function and COPD occurrence and the development of COPD among susceptile smokers, at variance with the so-called resistant smokers, would suggest that the weight of genetic risk factors is greater than recognized, In this paper the role of candidate genes for increasing the risk of COPD (such as α-proteinase inhibitor, α1-
antichymotrypsin, cystic fibrosis transmembrane conductance regulator, and others) is reviewed.

L43 ANSWER 28 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 94304084 EMBASE Full-text
DOCUMENT NUMBER: 1994304084
TITLE: Proteinase inhibitors in animal blood
with special regard to equine pulmonary disease: α1-proteinase inhibitor and
α2-macroglobulin.
AUTHOR: Pellegrini A.
CORPORATE SOURCE: Department of Veterinary Physiology, University of Zurich, Winterthurerstrasse 260,CH-8057 Zurich, Switzerland
SOURCE: Comparative Haematology International, (1994) Vol. 4, No. 3, pp. 121-129.
ISSN: 0938-7714 CODEN: CHAIEX
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
025 Hematology
LANGUAGE: English
ENTRY DATE: Entered STN: 941019
Last Updated on STN: 941019
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 29 OF 128 MEDLINE on STN
ACCESSION NUMBER: 94261982 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 8202851
TITLE: [The role of proteolytic enzyme inhibitors in the development and occurrence of chronic obstructive lung diseases].
Rol' ingibitorov proteoliticheskikh fermentov v razvitii i vozniknovenii khronicheskikh obstruktivnykh zabolevanii legkikh.
AUTHOR: Ubaidullaev A M; Kazakov K S; Liverko I V; Chernik M B
SOURCE: Terapevticheskii arkhiv, (1994) 66 (3) 42-5.
Journal code: 2984818R. ISSN: 0040-3660.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940714
Last Updated on STN: 19940714
Entered Medline: 19940707

L43 ANSWER 30 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 94111792 EMBASE Full-text
DOCUMENT NUMBER: 1994111792
TITLE: Pulmonary emphysema: Etiological mechanisms and therapeutic approaches.
AUTHOR: Turino G.M.
CORPORATE SOURCE: Department of Medicine, Columbia University, College of Physicians and Surgeons,New York, NY, United States
SOURCE: Drugs of Today, (1994) Vol. 30, No. 1, pp. 33-41.
ISSN: 0025-7656 CODEN: MDACAP
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 940504
Last Updated on STN: 940504
AB In the past three decades, significant progress has been made in the understanding of chronic obstructive lung disease from the standpoint of its clinical course, the etiological mechanisms of alveolar and bronchial injury, potential biochemical mechanisms of early detection of the disease and, most recently, therapies in the form of natural and synthetic inhibitors of neutrophil elastase which are approaching evaluation for clinical efficacy. In spite of this progress, chronic obstructive lung disease and its constituents of chronic bronchitis and emphysema remains a complex clinical entity of worldwide significance. There still remain crucial questions in our understanding of this disease, some of which have been listed in Table I. Hopefully, these are questions which will occupy the efforts of clinicians and investigators in the coming years, while we apply therapies from the knowledge already gained.

L43 ANSWER 31 OF 128 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 94052055 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7694273
TITLE: [Chronic obstructive lung disease and alpha-2-macroglobulin deficiency in serum--case report].
Chronisch-obstruktive Lungenerkrankung und alpha-2-Makroglobulin-Mangel im Serum--Kasuistik.
AUTHOR: Kruger U
CORPORATE SOURCE: Reha-Klinik der BfA, Utersum auf Fohr.
SOURCE: Pneumologie (Stuttgart, Germany), (1993 Sep) 47 (9) 531-4.
Journal code: 8906641. ISSN: 0934-8387.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117

Last Updated on STN: 19960129
Entered Medline: 19931217

AB The protease-antiprotease concept has contributed substantially to the pathogenetic understanding of different internistic disease patterns including the generalised, histologically mostly panlobular pulmonary emphysema. Attention is presently focused on alpha-1-antitrypsin protease inhibitor deficiency for which substitute solutions are already available. We present a case report on a patient of 40 years of age suffering from a severe, basally located pulmonary emphysema (as was evident on x-ray examination) with respiratory global insufficiency and an obstructive component that was only partially reversible under medication. Laboratory chemistry revealed that this was associated with an alpha-2-macroglobulin deficiency. Possibly the deficiency in this protease inhibitor of low specificity but broad spectrum of action may contribute to a better understanding of some of the types of emphysema that had so far been subclassified as cryptogenic although bearing traits of " proteinase inhibitor deficiency".

L43 ANSWER 32 OF 128 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 94044622 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8228125
TITLE: The molecular basis of alpha 1-antichymotrypsin deficiency in a heterozygote with liver and lung disease.
AUTHOR: Faber J P; Poller W; Olek K; Baumann U; Carlson J; Lindmark B; Eriksson S
CORPORATE SOURCE: Institut fur Klinische Biochemie, Universitat Bonn, Germany.
SOURCE: Journal of hepatology, (1993 Jul) 18 (3) 313-21.
Journal code: 8503886. ISSN: 0168-8278.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931214

AB Alpha 1-antichymotrypsin (alpha 1-ACT) is a serine proteinase inhibitor (serpin) with cathepsin G, mast cell chymase and chymotrypsin as target enzymes. We present the case of a middle-aged man with low plasma levels of alpha 1-ACT, asthma with progression to emphysema, and chronic HCV positive liver disease with selective accumulation of alpha 1-ACT in hepatocytes. This secretory defect is analogous to that seen in Pi Z alpha 1-antitrypsin deficiency. The molecular basis of alpha 1-ACT deficiency in this patient has been characterized by direct sequencing of the alpha 1-ACT genes from the patient and his father. A C-->G transversion in exon III causing a 229Pro-->Ala substitution is proposed to cause a conformational change resulting in abnormal transport through the RER. This mutation was found in one of 20 additional tested patients with chronic obstructive lung disease, but in no control. Two additional polymorphisms of the gene have been identified in unrelated healthy individuals with normal plasma alpha 1-ACT levels. The alpha 1-ACT deficiency state may predispose to obstructive lung disease and influence the course of liver disease. Identification of a specific mutation allows identification of heterozygotes for this deficiency allowing future evaluation of its clinical significance.

L43 ANSWER 33 OF 128 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 93379657 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8369790
TITLE: Bronchoalveolar lavage and the study of proteinases and antiproteinases in the pathogenesis of chronic obstructive lung disease.
AUTHOR: Stockley R A; Burnett D
CORPORATE SOURCE: Lung Immunobiochemical Research Laboratory, General Hospital, Birmingham, UK.
SOURCE: Monaldi archives for chest disease = Archivio Monaldi per le malattie del torace / Fondazione clinica del lavoro, IRCCS [and] Istituto di clinica tisiologica e malattie apparato respiratorio, Universita di Napoli, Secondo ateneo, (1993) 48 (3) 245-53. Ref: 82
Journal code: 9307314. ISSN: 1122-0643.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931029
Last Updated on STN: 20000303
Entered Medline: 19931014

AB Bronchoalveolar lavage has been used for 15 yrs to investigate the role of proteinases and antiproteinases in the pathogenesis of emphysema, but the results are confused by numerous technical factors, many of which may prove insurmountable. Even if the problems can be overcome, the technique will probably not prove sensitive enough to provide a true insight into the pathogenesis of emphysema in man. Nevertheless, the studies with this technique have provided important information and methodologies that have advanced our scientific, if not pathological, knowledge. Perhaps further applications of the knowledge obtained, to cellular and genetic studies, will eventually establish the true mechanisms involved in determining whether a smoker remains "healthy" or develops disabling disease. Lavage may have played a major role in the study of emphysema, if for no other reasons than to establish the fact that the pathogenesis of the disease is far from clear.

L43 ANSWER 34 OF 128 EMBASE
ACCESSION NUMBER: 92345813 EMBASE Full-text
DOCUMENT NUMBER: 1992345813
TITLE: Proteinase/proteinase inhibitor imbalance in sputum sol phases from patients with chronic obstructive pulmonary disease; Suggestions for a key role played by antileukoprotease.
AUTHOR: Piccioni P.D.; Kramps J.A.; Rudolphus A.; Bulgheroni A.; Luisetti M.
CORPORATE SOURCE: ITMAR, Universita degli Studi, Via Taramelli 5,27100 Pavia PV, Italy
SOURCE: Chest, (1992) Vol. 102, No. 5, pp. 1470-1476.
ISSN: 0012-3692 CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 921213
Last Updated on STN: 921213

AB In order to characterize the imbalance between proteinases and proteinase inhibitors in sputum sol phases, we studied 25 patients (mean age, 59±11 yr) with exacerbated chronic obstructive pulmonary disease (COPD). An aliquot of sputum was used for bacteriologic determinations, and the remainder was centrifuged in order to obtain gel and sol phases. On the basis of the bacteriologic data, patients were divided into colonized patients (14) and noncolonized patients (11). All of the major inhibitors were immunologically detectable in sol phases without a significant difference between colonized and noncolonized patients (α1-proteinase inhibitor [α1-PI], 2.56μM ± 0.53μM and 2.39μM ± 0.72μM; α2-macroglobulin [α2-MG], 0.21μM ± 0.07μM and 0.16μM ± 0.05μM; antileukoprotease (ALP), 1.78μM ± 0.57μM and 1.53μM ± 0.6μM, respectively [mean ± SE]). With regard to proteinase activities, both free elastase-like and free chymotrypsin-like activities were detectable in the majority of patients (15/25) (0.59μM ± 0.15μM and 0.74μM ± 0.15μM for elastase-like activity [ELA], and 0.010μM ± 0.003μM and 0.017μM ± 0.007μM for chymotrypsin-like activity [CLA], respectively [mean ± SE]). The inhibitory profile of proteinase activities, performed by means of a panel of inhibitors, allowed us to assign specific activities mainly to neutrophil elastase and cathepsin G (Cat G). Next we looked at the relationships between inhibitors and proteinase activities. We found a significant negative correlation between neutrophil elastase activity and ALP ($r = -0.58$; $p<0.01$). In confirmation of this suggestion, sol phases were divided into samples (15) with detectable ELA (>0.50μM) and samples (10) with no detectable ELA (<0.18μM). Levels of α1-PI and α2-MG did not differ significantly between the two groups, whereas ALP values were higher in the group with no detectable ELA (3.12μM ± 0.69μM) than in the other group (0.58μM ± 0.21μM; $p<0.001$). We conclude that most sputum sol phases from patients with exacerbated COPD have a high burden of free neutrophil elastase and Cat G. Antileukoprotease seems to be the major naturally occurring inhibitor effective in the modulation of proteinase activities in bronchial secretions under these conditions.

L43 ANSWER 35 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 92367351 EMBASE Full-text
DOCUMENT NUMBER: 1992367351
TITLE: Serum secretory leukoprotease inhibitor levels to diagnose pneumonia in the elderly.
AUTHOR: Kida K.; Mizuuchi T.; Takeyama K.; Hiratsuka T.; Jinno S.; Hosoda K.; Imaizumi A.; Suzuki Y.
CORPORATE SOURCE: Pulmonary Division, Tokyo Metropolitan Geriatric Hosp., 35-2 Sakae-cho,Itabashi, Tokyo 173, Japan
SOURCE: American Review of Respiratory Disease, (1992) Vol. 146, No. 6, pp. 1426-1429.
ISSN: 0003-0805 CODEN: ARDSBL
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 930110
Last Updated on STN: 930110

AB In pneumonia in the elderly, one occasionally encounters difficulties in evaluation with respect to both clinical observation and treatment. Thus a simple serum indicator is indicated. We measured secretory leukoprotease inhibitor (SLPI) concentrations in sera to see whether this can provide a useful indicator for pneumonia, especially in the elderly. Serum samples from patients over 65 yr of age, with (n = 54) or without (n = 87) pneumonia, and from healthy, young (n = 16) and aged (n = 188) control subjects were assayed using ELISA for human SLPI. Comparisons were made between groups with clinical diagnoses of either definite or probable pneumonia and among cases with various other respiratory diseases, including bronchial asthma, chronic obstructive pulmonary disease, and lung cancer. The mean SLPI concentration in patients with pneumonia was significantly higher than in patients without pneumonia or in healthy controls. The data suggest that the measurement of SLPI can provide a useful indicator for pneumonia to be used in clinical evaluation.

L43 ANSWER 36 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 92235341 EMBASE Full-text
DOCUMENT NUMBER: 1992235341
TITLE: Risk factors for reduced pulmonary function in women; A possible relationship between Pi phenotype, number of children, and pulmonary function.
AUTHOR: Horne S.L.; Chen Y.; Cockcroft D.W.; Dosman J.A.
CORPORATE SOURCE: Division of Respiratory Medicine, University Hospital,Saskatoon, Sask. 57N 0X0, Canada
SOURCE: Chest, (1992) Vol. 102, No. 1, pp. 158-163.
ISSN: 0012-3692 CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
017 Public Health, Social Medicine and Epidemiology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 920830
Last Updated on STN: 920830

AB Smoking and severe deficiency of protease inhibitor (Pi Z phenotype) both contribute significantly to the development of chronic obstructive pulmonary disease (COPD). The role of moderate Pi deficiency (Pi MZ phenotype) remains controversial. During a community-wide study of respiratory health which included 1,633 individuals, of whom 897 were women, we measured forced vital capacity (FVC), forced expired flow in 1 s (FEV1), midmaximum expired flow rate (MMFR), flow rate at 50 percent of FVC (V.ovrhdot.max50%) and flow rate at 25 percent of FVC above residual volume (V.ovrhdot.max25%). We carried out Pi phenotyping on 544 of these women, including 22 who were Pi MZ or FZ phenotypes. There were no statistically significant differences in mean pulmonary function (pf) values between the Pi MZ and Pi M women. Examination of residual pf values (difference between observed and expected) by means of multiple multivariate regression analysis revealed that in Pi MZ women, FEV1/FVC%, MMFR, V.ovrhdot.max50%, and V.ovrhdot.max25% had significantly greater values with increasing numbers of children, whereas there was no relationship in

the Pi M women. These results suggest that some factors may interact differently in individuals with Pi M and MZ phenotypes. In addition, the results suggest that pregnancy or pregnancy-induced increased Pi levels may have significant effects on the pulmonary health of Pi MZ women.

L43 ANSWER 37 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 92235335 EMBASE Full-text
DOCUMENT NUMBER: 1992235335
TITLE: Elevation of plasma truncated elastase α1-proteinase inhibitor complexes in patients with inflammatory lung diseases.
AUTHOR: Fujita J.; Nakamura H.; Yamagishi Y.; Yamaji Y.; Shiotani T.; Irino S.
CORPORATE SOURCE: 1st Department of Internal Medicine, Kagawa Medical School, 1950-1 Mikicho,Kita-gun, Kagawa 761-07, Japan
SOURCE: Chest, (1992) Vol. 102, No. 1, pp. 129-134.
ISSN: 0012-3692 CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 920830
Last Updated on STN: 920830

AB Human neutrophil elastase plays an important role in the development of several inflammatory lung diseases; however, there have been relatively few investigations using plasma samples. In this report, we describe alterations in the plasma elastase:α1-PI complex in patients with chronic obstructive pulmonary disease (COPD) (15 cases), COPD with infection (8), diffuse panbronchiolitis (DPB) (8), bronchiectasis (9), pneumonia (10), and the adult respiratory distress syndrome (ARDS) (14), and in 15 normal volunteers. The elastase:α1-PI complex concentration was determined by an enzyme-linked immunosorbent assay. Western immunoblot analysis of the elastase:α1-PI complex was also performed. Plasma elastase:α1-PI complex was also performed. Plasma elastase:α1-PI complex levels in patients with COPD with infection (504μg/L±93μg/L) were significantly higher, as compared with those with COPD but without infection (118μg/L±9μg/L) and normal volunteers (122μg/L±4μg/L). Increased complex concentrations were also found in patients with DPB and bronchiectasis (643μg/L±222μg/L and 558μg/L±198μg/L, respectively) as compared with normal volunteers. Increased complex concentrations were also found in patients with pneumonia and ARDS (450μg/L±101μg/L and 1,400μg/L±438μg/L, respectively). Western immunoblot analysis using anti-α1-PI antibody and antineutrophil elastase antibody showed two types of elastase:α1-PI complexes, one with a molecular weight of 60,000 daltons (60 kilodaltons [KD]) and the other at 50,000 daltons (50 KD). Although the native 80-KD elastase:α1-PI complex was detected in bronchoalveolar lavage fluid, it was not found in plasma. In summary, these results demonstrated that levels of the truncated complex were increased in patients with various inflammatory lung diseases. This truncated form may play an important role in the pathophysiology of inflammatory processes.

L43 ANSWER 38 OF 128 MEDLINE on STN

ACCESSION NUMBER: 93134862 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1485464
TITLE: [The treatment of acquired deficiency of alpha 1-proteinase inhibitor in the early stages of chronic obstructive lung diseases].
Lechenie priobretennogo defitsita al'fa 1-ingibitora proteinaz na rannikh stadiiakh khronicheskikh obstruktivnykh zabolevanii legkikh.
AUTHOR: Samokhina L M; Gladkov Iu G; Efimov V V
SOURCE: Likars'ka sprava / Ministerstvo okhorony zdorov'ia Ukrainy, (1992 Oct) (10) 97-100.
Journal code: 9601540. ISSN: 1019-5297.
PUB. COUNTRY: Ukraine
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199302
ENTRY DATE: Entered STN: 19930226
Last Updated on STN: 19970203
Entered Medline: 19930217

AB A new treatment scheme is proposed with a differential approach to correction of acquired deficiency of proteinase alpha-1 inhibitor. The treatment includes periodically repeated courses of antioxidant agents. In case of failure antioxidant agents are supplemented with courses of substitutive therapy by courses of proteolysis inhibitors up to normalization. Further treatment included repeated courses of antioxidant treatment for a more prolonged remission and prophylaxis of exacerbations.

L43 ANSWER 39 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 92132003 EMBASE Full-text
DOCUMENT NUMBER: 1992132003
TITLE: Animal models of chronic airways injury.
AUTHOR: Snider G.L.
CORPORATE SOURCE: United States
SOURCE: Chest, (1992) Vol. 101, No. 3 SUPPL., pp. 74S-79S.
ISSN: 0012-3692 CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
052 Toxicology
LANGUAGE: English
ENTRY DATE: Entered STN: 920524
Last Updated on STN: 920524
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 40 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 92277236 EMBASE Full-text
DOCUMENT NUMBER: 1992277236
TITLE: Ten-year changes of protease inhibitors in the sons of patients with COPD.
AUTHOR: Yoshioka A.; Nagata H.; Yamamoto M.; Akiyama Y.; Nishimura M.; Miyamoto K.; Kishi F.; Kawakami Y.
CORPORATE SOURCE: First Department of Medicine, Hokkaido University Sch. of Medicine, Sapporo, Japan
SOURCE: Annals of the New York Academy of Sciences, (1991) Vol. 624, pp. 359-361.
ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 921004
Last Updated on STN: 921004
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 41 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 92277216 EMBASE Full-text
DOCUMENT NUMBER: 1992277216
TITLE: Conference summary. Pulmonary emphysema: The rationale for therapeutic intervention.
AUTHOR: Cohen A.B.
CORPORATE SOURCE: University of Texas Health Center, P.O. Box 2003, Tyler, TX 75710, United States
SOURCE: Annals of the New York Academy of Sciences, (1991) Vol. 624, pp. 307-314.
ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis

017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
LANGUAGE: English
ENTRY DATE: Entered STN: 921004
Last Updated on STN: 921004
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 42 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 91318680 EMBASE Full-text
DOCUMENT NUMBER: 1991318680
TITLE: [The role of reactivation episodes in the pathogenesis of chronic obstructive lung disease].
IL RUOLO DEGLI EPISODI DI RIACUTIZZAZIONE DELLA PATOGENESI DELLE BRONCOPNEUMOPATIE CRONICHE OSTRUTTIVE.
AUTHOR: Ciaccia A.; Papi A.; Cogo A.
CORPORATE SOURCE: Clinica delle Malattie dell' Apparato Respiratorio, Universita degli Studi, Ferrara, Italy
SOURCE: Lotta Contro la Tuberculosi e le Malattie Polmonari Sociali, (1991) Vol. 61, No. 1, pp. 80-83.
ISSN: 0368-7546 CODEN: LCTUAK
COUNTRY: Italy
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: Italian
ENTRY DATE: Entered STN: 920305
Last Updated on STN: 920305
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 43 OF 128 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1992:78404 BIOSIS Full-text
DOCUMENT NUMBER: PREV199293046859; BA93:46859
TITLE: COMPARISON OF NORMAL SUBJECTS AND ASTHMA PATIENTS WITH RESPECT TO AGE-RELATED ELASTASE-BINDING ACTIVITY OF ALPHA-2 MACROGLOBULIN IN PLASMA.
AUTHOR(S): KILROE-SMITH T A [Reprint author]; BECKER P J; GAILLARD M C
CORPORATE SOURCE: NATIONAL CENTER OCCUPATIONAL HEALTH, PO BOX 4788, JOHANNESBURG, 2000 SOUTH AFRICA
SOURCE: Clinica Chimica Acta, (1991) Vol. 202, No. 1-2, pp. 47-54.
CODEN: CCATAR. ISSN: 0009-8981.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 2 Feb 1992
Last Updated on STN: 2 Feb 1992
AB Alpha-2-macroglobulin (α2M) is one of the major plasma protease inhibitors in adults. In our previous studies we have shown that it competes with α1-protease inhibitors for porcine pancreatic elastase (E.C. 3.4.21.11) when the latter is added to plasma. The binding of elastase by α1- protease inhibitor and α2M is of particular interest in studies on asthma, in view of the observation that elastase is capable of stimulating platelet activating factor (PAF) when it reacts with neutrophils. PAF causes hyper-reactivity of the airways and bronchoconstriction. Subseqeuntly we showed that the elastase binding capacity of α2M was higher in patients with chronic obstructive lung disease and emphysema and in patients with asthma than in normal individuals. Previous studies by other workers have shown a variation of α2-macroglobulin levels with age. Children have very high values, more than twice the adult level. Both these studies show a decrease in level in normal individuals, to reach a lower level in adulthood. Levine et al. relate this decrease to levels of dehydroepiandrosterone sulphate, the marker for biochemical adrenarche. No comparison has been done between normal individuals and asthmatics. In this paper we demonstrate that the variation of α2M with age, as indicated by its binding activity towards elastase, is different in asthmatics from that in normal subjects.

L43 ANSWER 44 OF 128 MEDLINE on STN
ACCESSION NUMBER: 90287275 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2192289
TITLE: [Elastase, elastase inhibitors and chronic

obstructive lung diseases].
Elastase, elastaseremmers en chronische obstructieve longziekten.
AUTHOR: Kramps J A; Dijkman J H
CORPORATE SOURCE: Academisch Ziekenhuis, afd. Longziekten, Leiden.
SOURCE: Nederlands tijdschrift voor geneeskunde, (1990 Jun 9) 134 (23) 1127-30. Ref: 25
Journal code: 0400770. ISSN: 0028-2162.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Dutch
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199007
ENTRY DATE: Entered STN: 19900824
Last Updated on STN: 20000303
Entered Medline: 19900726

L43 ANSWER 45 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 90043044 EMBASE Full-text
DOCUMENT NUMBER: 1990043044
TITLE: Serine proteinase inhibitors on chromosome 14 and the genetics of familial chronic obstructive airways disease.
AUTHOR: Kalsheker N.
CORPORATE SOURCE: Dept. of Medical Biochemistry, Univ. Wales Coll. of Medicine, Royal Infirmary, Newport Road,Cardiff CF2 1SZ, United Kingdom
SOURCE: Medical Hypotheses, (1990) Vol. 31, No. 1, pp. 67-70.
ISSN: 0306-9877 CODEN: MEHYDY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911213
Last Updated on STN: 911213
AB Environmental and genetic factors contribute to familial chronic obstructive airways disease. The genetic component could be polygenic or in some families be associated with one or two major genes. It is assumed that most cases of familial chronic obstructive airways disease are polygenic, but this conclusion is based on insufficient data. The use of linkage analysis using DNA probes for specific genes that may have a direct role in the disease process should facilitate our understanding of the genetics. Genetic deficiency of alpha1-antitrypsin is associated with predisposition to pulmonary emphysema. In the absence of alpha1-antitrypsin deficiency I suggest that a study of serine- proteinase inhibitors on chromosome 14 may identify a significant proportion of families where only one major gene is important.

L43 ANSWER 46 OF 128 MEDLINE on STN
ACCESSION NUMBER: 90253512 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2340047
TITLE: Long term effect on lung function of alpha 1-protease inhibitor substitution therapy in COPD patients with Pi ZZ phenotype.
AUTHOR: Ulmer W T; Schmidt E W; Rasche B
CORPORATE SOURCE: Medizinische Universitatsklinik, Berufsgenossenschaftlichen Krankenanstalten Bergmannsheil Bochum, Germany.
SOURCE: European respiratory journal. Supplement, (1990 Mar) 9 21s-22s.
Journal code: 8910681. ISSN: 0904-1850.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
ENTRY DATE: Entered STN: 19900720
Last Updated on STN: 19900720

Entered Medline: 19900627

AB Eight patients suffering from alpha 1-protease inhibitor (alpha 1-PI) deficiency (Pi ZZ phenotype) and chronic obstructive lung disease received substitution therapy (60 mg.kg-1 weekly) for a period of up to 30 months. Intrathoracic gas volume, airway resistance and arterial oxygen tension were followed once every three months. There was no trend for these indices to deteriorate or improve over the period of observation.

L43 ANSWER 47 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 90118912 EMBASE Full-text
DOCUMENT NUMBER: 1990118912
TITLE: Long term effect on lung function of alpha1-protease inhibitor substitution therapy in COPD patients with Pi ZZ phenotype.
AUTHOR: Ulmer W.T.; Schmidt E.W.; Rasche B.
CORPORATE SOURCE: Medizinische Universitatsklinik der Berufsgenossenschaftlichen Krankenanstalten 'Bergmannsheil Bochum', Gilsingstrasse 14, D-4630 Bochum, Germany
SOURCE: European Respiratory Journal, (1990) Vol. 3, No. SUPPL. 9, pp. 21s-22s.
ISSN: 0904-1850 CODEN: ERJOEI
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: French; English
ENTRY DATE: Entered STN: 911213
Last Updated on STN: 911213

AB Eight patients suffering from alpha1-protease inhibitor (alpha1-PI) deficiency (Pi ZZ phenotype) and chronic obstructive lung disease received substitution therapy (60 mg·kg-1 weekly) for a period of up to 30 months. Intrathoracic gas volume, airway resistance and arterial oxygen tension were followed once every three months. There was no trend for these indices to deteriorate or improve over the period of observation.

L43 ANSWER 48 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 89229151 EMBASE Full-text
DOCUMENT NUMBER: 1989229151
TITLE: [Clinical and pharmacokinetic evaluation for the replacement therapy of α1-protease-inhibitor (α1-PI) in patients with congenital α1-protease-inhibitor deficiency and lung emphysema].
KLINISCHE UND PHARMAKOKINETISCHE UNTERSUCHUNGEN ZUR SUBSTITUTION VON α1-PROTEASEN-INHIBITOR BEI PATIENTEN MIT HOMOZYGOTEM α1-PROTEASEN-INHIBITOR-MANGEL UND LUNGENEMPHYSEM.
AUTHOR: Schmidt E.W.; Derendorf H.; Rasche B.; Mollmann H.W.
CORPORATE SOURCE: Medizinische Klinik und Poliklinik, Berufsgenossenschaftliche Krankenanstalten 'Bergmannsheil', Universitatsklinik, D-4630 Bochum 1, United States
SOURCE: Atemwegs- und Lungenkrankheiten, (1989) Vol. 15, No. 9, pp. 479-488.
ISSN: 0341-3055 CODEN: ATLUDF
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
007 Pediatrics and Pediatric Surgery
015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911212
Last Updated on STN: 911212

DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 49 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 89145408 EMBASE Full-text
DOCUMENT NUMBER: 1989145408
TITLE: Chronic obstructive pulmonary disease: Risk factors, pathophysiology and pathogenesis.
AUTHOR: Snider G.L.
CORPORATE SOURCE: Medical Service, Boston VA Medical Center, Boston, MA 02130, United States
SOURCE: Annual Review of Medicine, (1989) Vol. 40, pp. 411-429.
ISSN: 0066-4219 CODEN: ARMCAH
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
035 Occupational Health and Industrial Medicine
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911212
Last Updated on STN: 911212

AB Chronic obstructive pulmonary disease (COPD) is defined in this chapter, and the relation between its two major components, (a) chronic bronchitis and emphysema and (b) nonremitting asthma, is discussed. Intensity of tobacco smoking and age are the major risk factors for the development of chronic airways obstruction. Environmental air pollution, childhood infections, and familial factors other than alpha-1 protease inhibitor deficiency appear to play only small roles. Emphysema is the major cause of severe airways obstruction; bronchiolitis is a contributing factor and likely is responsible for the minor reversible element of airways obstruction. The elastase-antielastase hypothesis, which is based mainly on indirect evidence, is the best explanation for the pathogenesis of emphysema. Extensive airspace enlargement with fibrosis is infrequently observed; this mechanism may play a role in the pathogenesis of the centrilobular emphysema of smokers.

L43 ANSWER 50 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 89206094 EMBASE Full-text
DOCUMENT NUMBER: 1989206094
TITLE: Detection of an alteration of the α2-macroglobulin gene in a patient with chronic lung disease and serum α2-macroglobulin deficiency.
AUTHOR: Poller W.; Barth J.; Voss B.
CORPORATE SOURCE: Medizinische Universitatsklinik, Klinikum Bergmannsheil, Ruhr-Universitat, D-4630 Bochum, Germany
SOURCE: Human Genetics, (1989) Vol. 83, No. 1, pp. 93-96.
ISSN: 0340-6717 CODEN: HUGEDQ
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911212
Last Updated on STN: 911212

AB α2-Macroglobulin (A2M) is a major human plasma protease inhibitor capable of inhibiting most endopeptidases tested so far. In the case of the other major plasma protease inhibitor , α1-antitrypsin, genetically determined deficiency states are known to increase the risk of chronic obstructive pulmonary disease (COPD) 20- to 30-fold in affected individuals. No defects of the A2M gene have been described as yet, but A2M may play a role in the regulation of protease activity in the lung, especially with respect to those proteases not inhibited by α1-antitrypsin. We report here the molecular genetic detection of an alteration of the A2M gene in a patient with serum A2M deficiency and chronic lung disease since childhood. The alteration involves restriction sites detected with 10 different enzymes and is most probably caused by a major deletion or rearrangement of the gene. Nine of the restriction enzymes used detected no polymorphisms in 40 healthy control subjects and 39 COPD patients. The polymorphism detected in this patient with the enzyme PvuII was different from another described previously, and was found in this patient only. The patient is heterozygous for an alteration in the A2M gene; this may be

responsible for his serum A2M deficiency and may be relevant to the early onset of pulmonary disease in his case.

L43 ANSWER 51 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 88097431 EMBASE Full-text
DOCUMENT NUMBER: 1988097431
TITLE: The flaccid lung syndrome and α1-protease inhibitor deficiency.
AUTHOR: Laros K.D.; Biemond I.; Klasen E.C.
CORPORATE SOURCE: Department of Human Genetics, Sylvius Laboratory, State University, 2333 AL Leiden, Netherlands
SOURCE: Chest, (1988) Vol. 93, No. 4, pp. 831-835.
ISSN: 0012-3692 CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911211
Last Updated on STN: 911211

AB We examined breathing mechanics and α1PI deficiency in 1,850 unrelated male subjects with various lung complaints. The loss in lung elasticity appeared to be significantly more pronounced in ZZ individuals as compared to MM, MS and also MZ individuals. The MZ group did not differ significantly in this respect from MM individuals. This implies that the excess risk of developing a flaccid lung (C>1 kPa-a1) due to the partial α1-antitrypsin deficiency is negligible. PI MZ and PI ZZ frequencies are significantly higher in the population with flaccid lung compared to control subjects. Furthermore, it was found that the increase in residual volume in smokers is independent of the PI type.

L43 ANSWER 52 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 88050187 EMBASE Full-text
DOCUMENT NUMBER: 1988050187
TITLE: Emphysema of early onset associated with a complete deficiency of alpha-1-antitrypsin (null homozygotes).
AUTHOR: Cox D.W.; Levison H.
CORPORATE SOURCE: Research Institute, The Hospital for Sick Children, Toronto, Ont. M5G 1X8, Canada
SOURCE: American Review of Respiratory Disease, (1988) Vol. 137, No. 2, pp. 371-375.
ISSN: 0003-0805 CODEN: ARDSBL
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911211
Last Updated on STN: 911211

AB We have compared lung function in 3 subjects with no α1-antitrypsin (α1-protease inhibitor) (null homozygotes) with subjects having the typical deficiency, PI ZZ. We identified a 31-yr-old woman, presenting with severe obstructive lung disease, who had no detectable plasma α1-antitrypsin indicating homozygosity for a 'null' (or PI(*)QO) allele of α1-antitrypsin. Two of her sisters have a similar deficiency, one with an onset of symptoms at 17 yr of age. Because of the likelihood that there are a number of different PI(·)QO alleles, the type in this family has been named null Mattawa (QOmattawa). All 3 homozygotes have shown a marked deterioration of lung function over a 7-yr period of follow-up. In contrast, lung function tests of 6 age-matched nonsmoking subjects with α1-antitrypsin deficiency, PI type ZZ, showed no abnormalities of lung function. The 15 to 20% of the normal plasma concentration of α1-antitrypsin associated with PI(*) Z allele appears to provide some protection to the lung in comparison with a complete deficiency state.

L43 ANSWER 53 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 88210704 EMBASE Full-text
DOCUMENT NUMBER: 1988210704
TITLE: Study of serum alpha1 antitrypsin levels and protease inhibitor system in Korean patients with chronic obstructive pulmonary diseases.
AUTHOR: Koh Y.S.; Yun H.J.; Lew W.J.; Park S.S.; Lee J.H.
CORPORATE SOURCE: Department of Internal Medicine, College of Medicine, Hanyang University, Seoul, Korea, Republic of
SOURCE: Tuberculosis and Respiratory Diseases, (1988) Vol. 35, No. 2, pp. 110-119.
CODEN: KHCHAM
COUNTRY: Korea, Republic of
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: Korean
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911211
Last Updated on STN: 911211
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 54 OF 128 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 88250271 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 3289388
TITLE: Replacement therapy for alpha-1-protease inhibitor deficiency in PiZ subjects with chronic obstructive lung disease.
AUTHOR: Schmidt E W; Rasche B; Ulmer W T; Konietzko N; Becker M; Fallise J P; Lorenz J; Ferlinz R
CORPORATE SOURCE: Bergmannsheil Hospital, Bochum, Federal Republic of Germany.
SOURCE: American journal of medicine, (1988 Jun 24) 84 (6A) 63-9.
Journal code: 0267200. ISSN: 0002-9343.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198807
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 20000303
Entered Medline: 19880722

AB In a six-month multicenter feasibility and safety study, 20 patients, who all had a congenital deficiency of alpha-1-protease inhibitor (A1PI) of the PiZ phenotype accompanied by a chronic obstructive lung disease, were treated with human-plasma-derived A1PI. A weekly dose of 60 mg/kg, administered intravenously, was shown to be sufficient to maintain patient serum levels above the threshold limit of 35 percent, the serum level of healthy persons of the MZ phenotype. This is supposed to be the minimal effective level for protection against the elastolytic attack of the lung and, therefore, satisfies one of the most important criteria of feasibility of long-term replacement therapy. The global concentration in serum or bronchiolar lavage fluid A1PI including active and inactivated A1PI was measured immunologically by rate nephelometry and radial immunodiffusion. The functional activity of A1PI, expressed as free inhibitor activity against trypsin and leukocyte elastase, confirmed that the infused A1PI remained mostly in its active form in the circulation. Reported adverse reactions were moderate and did not require alteration to the schedule of the infusions and/or the dose and rate of administration. Antibodies to A1PI as measured by the Ouchterlony method did not develop. Laboratory and physical signs of possible hepatitis virus contamination were not observed. The long-term replacement therapy, therefore, appears to be safe.

L43 ANSWER 55 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 88001380 EMBASE Full-text
DOCUMENT NUMBER: 1988001380

TITLE: Transpulmonary difference of α1 protease inhibitor (α1 PI) and polymorphonuclear (PMN) elastase-α1 PI complex in chronic lung diseases (Rapid communication).
AUTHOR: Ishizaki T.; Azuma H.; Takahashi H.; AmeJima S.; Kishi Y.; Sasaki F.; Miyabo S.
CORPORATE SOURCE: The Third Department of Internal Medicine, Fukui Medical School, Fukui 910-11, Japan
SOURCE: Respiration Research, (1987) Vol. 6, No. 11, pp. 1274-1277.
ISSN: 0286-9314 CODEN: KOKUDH
COUNTRY: Japan
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: Japanese
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911211
Last Updated on STN: 911211
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 56 OF 128 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 7
ACCESSION NUMBER: 1988:34132 BIOSIS Full-text
DOCUMENT NUMBER: PREV198885021857; BA85:21857
TITLE: STUDIES ON THE TURNOVER OF METHIONINE OXIDIZED ALPHA-1 PROTEASE INHIBITOR IN RATS.
AUTHOR(S): GLASER C B [Reprint author]; KARIC L; PARMELEE S; PREMACHANDRA B R; HINKSTON D; ABRAMS W R
CORPORATE SOURCE: CODON, 430 VALLEY DRIVE ROAD, BRISBANE, CALIF 94005, USA
SOURCE: American Review of Respiratory Disease, (1987) Vol. 136, No. 4, pp. 857-861.
CODEN: ARDSBL. ISSN: 0003-0805.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 28 Dec 1987
Last Updated on STN: 28 Dec 1987
AB Alpha-1-protease inhibitor (alpha-1-PI) is the major regulator of extracellular leukocyte elastase activity and can be rendered impotent against elastase by oxidation of a critical methionine, residue 358. Alpha-1-PI was isolated from rat plasma by affinity chromatography on Sepharose-bound anhydrochymotrypsin, DEAE-cellulose anion-exchange, and Sephadex G-150 gel filtration. The product was radiolabeled using non-oxidative conditions with Bolton-Hunter reagent, and an alliquot subsequently oxidized with N-chlorosuccinimide. Turnover studies in rats indicated that both native and oxidized alpha-1-PI had half-lives of 170 min. Using partially purified human neutrophil methionine sulfoxide-peptide reductase (Met(O)PR). It was demonstrated that oxidized product could be converted back "in vitro" to an active inhibitor of elastase. To assess whether oxidized alpha-1-PI underwent reduction "in vitro", methionine-oxidized rat inhibitor was injected into the rats, aliquots of plasma samples were withdrawn and passed through a Sepharose-bound anhydrochymotrypsin affinity resin, and bound functional alpha-1-PI was eluted with 0.1 M chymostatin. Radioactive counting of bound and unbound fractions indicated that reduction does not occur in vivo and suggested that, at least under homeostatic conditions, the Met(O)PR is confined to intracellular sites where it does not have access to the circulating protein.

L43 ANSWER 57 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 87080115 EMBASE Full-text
DOCUMENT NUMBER: 1987080115
TITLE: Lung lavage fluid from patients with α1-proteinase inhibitor deficiency or chronic obstructive bronchitis: Anti-elastase function and cell profile.
AUTHOR: Morrison H.M.; Kramps J.A.; Burnett D.; Stockley R.A.
CORPORATE SOURCE: Lung Immunobiochemical Research Laboratory, General Hospital, Birmingham B4 6NH, United Kingdom
SOURCE: Clinical Science, (1987) Vol. 72, No. 3, pp. 373-381.
CODEN: CSCIAE
COUNTRY: United Kingdom

DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
005 General Pathology and Pathological Anatomy
LANGUAGE: English
ENTRY DATE: Entered STN: 911211
Last Updated on STN: 911211

AB The anti-elastase composition of broncho-alveolar lavage (BAL) fluid from α1-proteinase inhibitor (α1PI) deficient and bronchitic patients was determined by immunological and functional assays, together with the cell profile of the BAL fluid. α1PI, anti-leucoprotease and α2-macroglobulin were present in all the samples. BAL fluid α1PI concentrations were significantly lower in the group with serum α1PI deficiency. Lavage fluid from α1PI subjects inhibited less porcine pancreatic elastase than bronchitic BAL fluid (P<0.005). However, the α1PI was only about 50% active as an inhibitor in both groups. There was no difference in the amount of neutrophil elastase (NE) inhibited per ml of lavage fluid or per mol of the measured inhibitors in the secretions, but both groups inhibited more enzyme than would be expected for these inhibitors (α1PI deficient: median 4.78 mol of NE/mol of known inhibitors, range 0.88-78.80; bronchitic: 1.14, 0.21-4.66), suggesting that an additional inhibitor is present. The total leucocyte and neutrophil counts were elevated (2P<0.01) in the lavages of α1PI deficient patients, suggesting a greater potential elastase burden than subjects with normal α1PI.

L43 ANSWER 58 OF 128 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1988:104380 BIOSIS Full-text
DOCUMENT NUMBER: PREV198834050722; BR34:50722
TITLE: CONCENTRATION OF THE BRONCHIAL INHIBITOR IN SERUM OF IRON MINERS EFFECT OF SMOKING AND ALPHA-PI PHENOTYPE.
AUTHOR(S): TOURNIER J M [Reprint author]; PIERRE F; PHAM Q T
CORPORATE SOURCE: INSERM UNITES 14, INRS, VANDOEUVRE-LES-NANCY, FR
SOURCE: Clinical Respiratory Physiology, (1987) Vol. 23, No. SUPPL. 12, pp. 328S.
Meeting Info.: SYMPOSIUM ON THE MECHANISMS AND MANAGEMENT OF RESPIRATORY SYMPTOMS HELD AT THE 22ND ANNUAL MEETING OF THE SOCIETAS EUROPAEA PHYSIOLOGIAE CLINICAE RESPIRATORIAE (EUROPEAN SOCIETY OF CLINICAL RESPIRATORY PHYSIOLOGY), ANTWERP, BELGIUM, JUNE 22-26, 1987. CLIN RESPIR PHYSIOL.
CODEN: CRPHD4. ISSN: 0272-7587.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 17 Feb 1988
Last Updated on STN: 17 Feb 1988

L43 ANSWER 59 OF 128 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 8
ACCESSION NUMBER: 1987:365433 BIOSIS Full-text
DOCUMENT NUMBER: PREV198733055908; BR33:55908
TITLE: ALPHA-1 PROTEINASE INHIBITOR A EUROPEAN OVERVIEW.
AUTHOR(S): ROBALO-CORDEIRO A J A [Reprint author]
CORPORATE SOURCE: DEP OF CENT OF PNEUMOLOGY, UNIV OF COIMBRA, 3049 COIMBRA CODEX, PORTUGAL
SOURCE: European Journal of Respiratory Diseases, (1987) Vol. 70, No. 5, pp. 261-265.
CODEN: EJRDD2. ISSN: 0106-4339.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 29 Aug 1987
Last Updated on STN: 29 Aug 1987

L43 ANSWER 60 OF 128 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1987:337269 BIOSIS Full-text
DOCUMENT NUMBER: PREV198784046212; BA84:46212
TITLE: STUDY OF FAMILIAL ALPHA-1 PROTEINASE INHIBITOR DEFICIENCY INCLUDING A RARE

PROTEINASE INHIBITOR PHENOTYPE IZ I.
ALPHA-1-PHENOTYPING AND CLINICAL INVESTIGATIONS.

AUTHOR(S): BAUR X [Reprint author]; BENCZE K
CORPORATE SOURCE: MEDIZINISCHE KLINIK I, KLINIKUM GROSSHADERN, POSTFACH 70 12 60, D-8000 MUENCHEN 70, FRG

SOURCE: Respiration, (1987) Vol. 51, No. 3, pp. 188-195.
CODEN: RESPBD. ISSN: 0025-7931.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 8 Aug 1987
Last Updated on STN: 8 Aug 1987

AB Proteinase inhibitor (PI) phenotyping and clinical investigations were performed on 20 persons in three generations of a family with α1-antitrypsin deficiency. Two persons were homozygotes and 9 were heterozygotes for the Z allele; one is the first reported IZ phenotype; 11 were common M-types. Both homozygotes and 5 of the heterozygotes, including the IZ individual, had suffered from recurring or chronic respiratory diseases. However, only mild to moderate impairment in lung function tests was observed in some of these patients (DLCO steady state, 3 subjects; FEV1, 3 subjects; FEF25-75, 2 subject; elevation of RV, 2 subjects). The rare IZ type, a 35-year-old female, smoker, showed normal lung function except for an elevated RV. Our results indicate that PI deficiency is not necessarily associated with severe lung destruction if noxious inhalants are absent.

L43 ANSWER 61 OF 128 EMBASE

ACCESSION NUMBER: 87146972 EMBASE Full-text
DOCUMENT NUMBER: 1987146972

TITLE: Elastase inhibitors in sputum from bronchitic patients with and without α1-proteinase inhibitor deficiency: Partial characterization of a hitherto unquantified inhibitor of neutrophil elastase.

AUTHOR: Morrison H.M.; Kramps J.A.; Afford S.C.; et al.
CORPORATE SOURCE: Lung Immunobiochemical Research Group, General Hospital, Birmingham B4 6NH, United Kingdom

SOURCE: Clinical Science, (1987) Vol. 73, No. 1, pp. 19-28.
CODEN: CSCIAE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
025 Hematology
LANGUAGE: English
ENTRY DATE: Entered STN: 911211
Last Updated on STN: 911211

AB 1. Anti-elastase function in sputum sol-phase from patients with α1-proteinase inhibitor (α1PI) deficiency was compared with sol-phase from patients with cigarette smoke-induced bronchitis and emphysema. 2. Both α1PI (2P < 0.01) and anti-leucoprotease (ALP) (2P < 0.01) concentrations were lower in sol-phase from the α1PI-deficient group, although α2-macroglobulin (α2M) levels were similar. 3. There was no difference in α1PI function between the two groups, but the inhibitor was only .simeq.30% active. 4. The absolute neutrophil elastase (NE) inhibitory capacity was similar in both groups (median 185 μg of NE inhibited/ml of sputum, range 80-480, for the α1PI-deficient group; median 175, range 80-300, for the bronchitic group). A substantial proportion of NE inhibition in secretions could not be accounted for by the amount of α1PI, ALP and α2M present (median 74.8%, range 43.2-97.4, for α1PI-deficient sol-phase; median 50.0%, range 0-80.8, for bronchitic sol-phase). 5. Gel filtration of sol-phase demonstrated the presence of NE inhibition in the low molecular weight fractions which was markedly sensitive to changes in substrate concentration and ionic strength, in contrast to purified α1PI and ALP. 6. Sputum sol-phase from both groups failed to prevent hydrolysis of elastin-fluorescein or succinyltrialanyl-p-nitroanilide by NE completely during prolonged incubation in the presence of an excess of function inhibitors. This was more apparent in secretions from subjects with α1PI deficiency and may explain why such patients have a more rapidly progressive form of emphysema.

L43 ANSWER 62 OF 128 EMBASE

ACCESSION NUMBER: 86168237 EMBASE Full-text

DOCUMENT NUMBER: 1986168237
TITLE: Elastase inhibitors of sputum sol phase: Variability, relationship to neutrophil elastase inhibitor, and effect of corticosteroid treatment.
AUTHOR: Stockley R.A.; Morrison H.M.; Kramps J.A.; et al.
CORPORATE SOURCE: Lung Immunobiochemical Research Laboratory, General Hospital, Birmingham B4 6NH, United Kingdom
SOURCE: Thorax, (1986) Vol. 41, No. 6, pp. 442-447.
CODEN: THORA7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 911210
Last Updated on STN: 911210

AB The concentrations of three known elastase inhibitors (α1 proteinase inhibitor, antileucoprotease, and α2 macroglobulin) have been determined in the sputum of six patients with obstructive bronchitis over five consecutive days. Antileucoprotease was the major inhibitor measured and potentially could provide more than 80% of the elastase inhibition, whereas the contribution of α2 macroglobulin was less than 0.2%. Comparison with the inhibitory capacity of the secretions active against human neutrophil elastase showed that the inhibitors could account for only about half of the inhibition measured. This suggests the presence of a substantial amount of unrecognised inhibitor. Corticosteroid treatment in 10 patients reduced the mean α1 proteinase inhibitor concentration ($p < 0.025$) from 18.6 μg/ml (SD 22.5) to 9.8 (6.6). Antileucoprotease, however, increased ($p < 0.05$) from 20.5 μg/ml (24.3) to 39.3 (23.4). These changes were associated with an increase in elastase inhibition ($p < 0.025$) from 180 (160) μg elastase/ml secretion to 310 (130), suggesting a beneficial effect of steroid treatment on the antielastases in lung secretions.

L43 ANSWER 63 OF 128 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:512988 CAPLUS Full-text
DOCUMENT NUMBER: 105:112988
TITLE: Is antioxidant deficiency related to chronic obstructive pulmonary disease?
AUTHOR(S): Taylor, Joseph C.; Madison, Roberta; Kosinska, Daniela
CORPORATE SOURCE: Dep. Respir. Dis., City of Hope Med. Cent., Duarte, CA, 91010, USA
SOURCE: American Review of Respiratory Disease (1986), 134(2), 285-9
CODEN: ARDSBL; ISSN: 0003-0805
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An assay with the capability of detecting antioxidant activity of plasma and of purified proteins is described. The method is based on the enzymic oxidation of plasma elastase inhibitory capacity by enzyme(s) in exts. of human lysosomes in the presence of hydrogen peroxide, chloride, and Mg ions. Using this method, the antioxidant activity of the plasma of 59 subjects was measured. A strong relationship was detected between a deficiency in the antioxidant activity of plasma and the presence of a family history of lung disease and an abnormal mean forced expiratory volume in 1 s to forced vital capacity ratio.

L43 ANSWER 64 OF 128 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 86201432 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 3009960
TITLE: [Alpha 1-antitrypsin deficiency: a review with special reference to the significance of heterozygous deficiency]. Alpha-1-Antitrypsin-Mangel. Eine Ubersicht unter besonderer Berucksichtigung der Bedeutung des heterozygoten Mangels.
AUTHOR: Schneider M; Pott G; Gerlach U
SOURCE: Klinische Wochenschrift, (1986 Mar 3) 64 (5) 197-205.
Journal code: 2985205R. ISSN: 0023-2173.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals

ENTRY MONTH: 198606
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860609

AB Homozygous deficiency of alpha-1 antitrypsin is the most common inborn error or metabolism in Europe. Severe deficiency of this major protease inhibitor in serum is associated with chronic obstructive lung disease, chronic liver disease in adults and neonatal hepatitis. An overview is given of the role of heredity, and the diagnostic criteria and clinical and histological findings in this disorder. Emphysema seems to be caused by the free elastolytic activity of white cells, leading to the degradation of elastin. The pathophysiology of liver disease - less well understood - is discussed with special emphasis on the importance of heterozygous alpha-1 antitrypsin deficiency. Exogenous noxae seem to play an important role in the pathogenesis of heterozygous deficiency. In view of the 7% frequency of heterozygous alpha-1 antitrypsin deficiency in the European population and the role of noxae in the development of pulmonary and liver diseases, improved prophylaxis is mandatory.

L43 ANSWER 65 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 86115394 EMBASE Full-text
DOCUMENT NUMBER: 1986115394
TITLE: Increased serum levels of α-2-macroglobulin in severe Chronic Airflow Obstruction.
AUTHOR: Pedersen J.Z.; Franck C.
CORPORATE SOURCE: Medical Department B, Rigshospitalet, Copenhagen, Denmark
SOURCE: European Journal of Respiratory Diseases, (1986) Vol. 68, No. 3, pp. 195-199.
CODEN: EJRDD2
COUNTRY: Denmark
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
025 Hematology
023 Nuclear Medicine
LANGUAGE: English
SUMMARY LANGUAGE: French
ENTRY DATE: Entered STN: 911210
Last Updated on STN: 911210

AB Serum levels of α-2-macroglobulin, the major proteinase inhibitor besides α-1-antitrypsin, were investigated in 20 patients with severe Chronic Airflow Obstruction (CAO), as compared to 20 age- and sex-matched controls. α-2-macroglobulin was assessed by rocket immuno-electrophoresis, and α-1-antitrypsin by a laser-nephelometric method. All patients had spirometric values determined, including diffusing capacity. The reversibility test for isoprenalin was performed. α-2-macroglobulin levels were found to be significantly elevated in patients with CAO, even when two patients with α-1-antitrypsin deficiency were omitted from the statistical evaluation. Except for these two patients, there was no difference in α-1-antitrypsin level between the patients and the control group. It is concluded that elevated levels of α-2-macroglobulin are associated with the development of severe CAO and emphysematous lesions, also in the absence of α-1-antitrypsin deficiency.

L43 ANSWER 66 OF 128 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:108928 CAPLUS Full-text
DOCUMENT NUMBER: 102:108928
TITLE: Determination of oxidized α-1-proteinase inhibitor in serum or plasma
INVENTOR(S): Travis, James
PATENT ASSIGNEE(S): University of Georgia Research Foundation, Inc., USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4493891	A	19850115	US 1982-402442	19820727

US 4605616 A 19860812 US 1984-654966 19840927
PRIORITY APPLN. INFO.: US 1982-402442 A1 19820727

AB A method for determining the percentage of oxidized α-1-proteinase inhibitor (I) in human blood serum or plasma is presented which involves (1) determining the activities of an enzyme inhibitable by I and an elastase in the presence of the unknown sample; (2) determining the activities of the I-inhibitable enzyme and elastase in standard solns.; (3) determining the oxidized ratio, Ko of the unknown sample by the equation Ko = (Tk-Tu)/(Ek-Eu), where Tk and Tu are the activities of the I-inhibitable enzyme in the standard and unknown samples, resp., and Ek and Eu are the elastase activities in the standard and unknown samples, resp.; (4) determining the reduced ratio; Kr, of a standard reduced sample of plasma or serum by the equation Kr = (Tk-Rr)/(Ek-Er), where Tr and Er are the I-inhibitable enzyme and elastase activities, resp., in the standard reduced sample and Tk and Ek are as defined above.; (5) determining the percent oxidized I, X, from the equation X = (1-Kr/K0) + 100. Thus, the activities of stock solns. of trypsin and elastase were determined in 0.05M Tris-HCl buffer, pH 8.0 by standard methods. N-Benzoyl-L-arginine Et ester was used as the trypsin substrate and succinyl-L-alanyl-L-alanyl-L-alanyl-p-nitroanilide was used as the elastase substrate. Next, the activities of these 2 enzymes were determined both in the presence of a known amount of I and an aliquot of serum (I amount unknown), and Ko was calculated The activities were then determined in the presence of a known amount of mercaptoethanol-reduced I, and Kr and X were calculated With this assay, it was shown that 23% of I in the serum of smokers was oxidized. This method can be used with patients having a potential for chronic obstructive lung disease as an alternative to bronchial lavage methods.

L43 ANSWER 67 OF 128 EMBASE
ACCESSION NUMBER: 85166854 EMBASE Full-text
DOCUMENT NUMBER: 1985166854
TITLE: Utilization of a peroxidase antiperoxidase complex in an enzyme-linked immunosorbent assay of elastin-derived peptides in human plasma.
AUTHOR: Kucich U.; Christner P.; Lippmann M.; et al.
CORPORATE SOURCE: Anatomy Department, School of Dental Medicine, Philadelphia, PA 19104, United States
SOURCE: American Review of Respiratory Disease, (1985) Vol. 131, No. 5, pp. 709-713.
CODEN: ARDSBL
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
026 Immunology, Serology and Transplantation
LANGUAGE: English
ENTRY DATE: Entered STN: 911210
Last Updated on STN: 911210

AB Chronic obstructive pulmonary disease (COPD), a major cause of morbidity and death in the smoking population, develops insidiously over many years, and significant impairment of lung function usually occurs before the disease is diagnosed. Because lung elastin degradation appears to be a prerequisite for the development of the disease, immunologic detection of elastin-derived peptides in the blood might be an effective approach to the early detection and monitoring of the disease. We here report an improved enzyme-linked immunosorbent assay for elastin peptides using a peroxidase-antiperoxidase complex as the reporter group. The assay is sensitive to 2 ng/ml elastin peptides. We show that for optimal, reproducible results the assay should be carried out at 16° C rather than at room temperature and that determinations should be made on plasma containing protease inhibitors rather than on serum. The levels of elastin-derived peptides appeared to remain relatively constant when multiple samples were taken during 5- to 10-wk period from individual subjects. In addition, patients with COPD had elevated elastin peptide levels (127 ± 47 ng/ml) compared with levels in normal nonsmokers (58 ± 17 ng/ml), whereas normal smokers had values intermediate between the 2 groups (mean peptide levels of 76 ± 42 ng/ml). A small group of normal smokers (20%) had elevated elastin peptide levels similar to those in the emphysema group and may represent that group of smokers who are at risk of developing obstructive lung disease.

L43 ANSWER 68 OF 128 EMBASE
ACCESSION NUMBER: 86020104 EMBASE Full-text
DOCUMENT NUMBER: 1986020104
TITLE: Effect of smoking on peripheral blood leukocytes and serum

antiproteases.
AUTHOR: Bridges R.B.; Wyatt R.J.; Rehm S.R.
CORPORATE SOURCE: Department of Oral Biology, College of Medicine and Dentistry, University of Kentucky, Lexington, KY 40536, United States
SOURCE: European Journal of Respiratory Diseases, (1985) Vol. 66, No. SUPPL. 139, pp. 24-33.
CODEN: EJRDD2
COUNTRY: Denmark
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
025 Hematology
029 Clinical Biochemistry
006 Internal Medicine
052 Toxicology
LANGUAGE: English
ENTRY DATE: Entered STN: 911210
Last Updated on STN: 911210

AB Cigarette smokers have an increased risk of chronic obstructive airways disease which has been attributed to a protease-antiprotease imbalance in the lung. The neutrophil is an important source of proteases as well as of myeloperoxidase, which oxidatively inactivates α-1- proteinase inhibitor (α-1-PI). The purpose of this study is to evaluate the protease-antiprotease imbalance hypothesis by measuring changes in peripheral blood components in a group of 110 young, male, asymptomatic smokers and an equal number of age-matched non-smokers. Significant (p=0.001), but modest impairment of pulmonary function was observed in the smokers as measured by both forced expiratory spirometry and the single breath nitrogen test. A 35% increase (p=0.0001) in peripheral blood leukocytes in smokers was attributable to increases in neutrophils (44%), lymphocytes (31%) and monocytes (23%). This increase in leukocyte count correlated significantly (p≤0.01) with some of the more sensitive indicators of airway obstruction (FEV1/FVC, CV/VC, CC/TLC, and ΔN2/L). Myeloperoxidase activity of neutrophils isolated from peripheral blood of smokers was 13% higher than in non-smokers, while elastase activity per neutrophill was apparently unaffected by smoking. In 50 subject pairs, elevations in serum α-1-PI concentrations in smokers (13.7%) were comparable to similar increases in trypsin (9.9%) and elastase (12.4%) inhibitory capacities. Expressed as nanomoles protease inhibited per nanomole of α-1-PI, the apparent functional activity of α-1-PI was unaltered by smoking. However, a lower, apparent functional activity of α-1-PI against trypsin and elastase was observed in both smokers and non-smokers with higher serum α-1-PI concentrations. Thus, in a population of young smokers, changes in leukocyte count, neutrophil lysosomal enzyme activities, and functional serum antiprotease activity appear to be consistent with the establishment of a protease-antiprotease imbalance. This imbalance may predispose these smokers to obstructive lung disease.

L43 ANSWER 69 OF 128 EMBASE
ACCESSION NUMBER: 85032527 EMBASE Full-text
DOCUMENT NUMBER: 1985032527
TITLE: Elastin: Relation of protein and gene structure to disease.
AUTHOR: Rosenbloom J.
CORPORATE SOURCE: Center for Oral Health Research, School of Dental Medicine, University of Pennsylvania, Philadelphia, PA 19104, United States
SOURCE: Laboratory Investigation, (1984) Vol. 51, No. 6, pp. 605-623.
CODEN: LAINAW
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
013 Dermatology and Venereology
011 Otorhinolaryngology
022 Human Genetics
029 Clinical Biochemistry
015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
ENTRY DATE: Entered STN: 911210
Last Updated on STN: 911210

AB The elastic properties of many tissues such as the lung, dermis, and large blood vessels are due to the presence of elastic fibers in the extracellular space. These fibers have been shown by biochemical and ultrastructural analysis to be comprised of two distinct

components, a more abundant amorphous component and the microfibrillar component. The microfibrillar component is found in 10 to 12-nm fibrils which are located primarily around the periphery of the amorphous component but, to some extent, interspersed within it. The protein, elastin, makes up the highly insoluble amorphous component and is responsible for the elastic properties. Elastin is found throughout the vertebrate kingdom except for very primitive fish and possesses an unusual chemical composition consonant with its characteristic physical properties. Elastin is composed largely of glycine, proline, and other hydrophobic residues and contains multiple lysine-derived cross-links, such as the desmosines, which link the individual polypeptide chains into a rubber-like network. The intervening, hydrophobic regions of the polypeptide chains between the cross-links are highly mobile, and the elastic properties of the fibers can be described in terms of the theory of rubber elasticity. Recent application of recombinant DNA techniques has led to further understanding of the structure of elastin. Analyses of the bovine and human elastin genes have demonstrated that the hydrophobic and cross-linking domains are encoded in separate exons. These exons tend to be small, varying from 27 to 114 base pairs, and are separated by large intervening sequences. Furthermore, DNA sequence analysis has demonstrated that the elastin molecule contains two cysteine residues which were not previously identified near the carboxy terminus and which may be important in the interaction of elastin with other extracellular matrix proteins. Further DNA sequencing should determine the complete amino acid sequence of elastin. Biosynthetic studies and in vitro translation of elastin mRNA have demonstrated that a 72,000-dalton polypeptide, designated tropoelastin, is the initial translation product. Analysis of several developing systems has demonstrated that elastin synthesis is controlled by the level of elastin mRNA. After packaging into membrane-bound vesicles in the Golgi apparatus, tropoelastin is secreted by exocytosis into the extracellular space where it is cross-linked by a copper-requiring extracellular enzyme, lysyl oxidase. Elastin can be solubilized only by proteases that have consequently been designated elastases, although these are general, powerful proteases than can hydrolyze numerous proteins. The elastase secreted by leukocytes is a serine protease inhibitable by α1 protease inhibitor, whereas the elastase secreted by macrophages is a metalloprotease not inhibitale by α1 protease inhibitor. Degradation of elastin by these elastases may be central to the pathogenesis of chronic obstructive lung disease and some vascular diseases. Although no heritable diseases have as yet been shown to be caused by molecular defects of elastin, several diseases, including the Marfan syndrome, pseudoxanthoma elasticum, and the Buschke-Ollendorf syndrome, may result from such defects. Studies utilizing cloned genomic, human elastin DNA may lead to definition of genetic alterations. Similar studies of polymorphism of the elastin gene in the normal population may identify variants that increase the susceptibility to acquired diseases that affect elastic connective tissue.

L43 ANSWER 70 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 85014870 EMBASE Full-text
DOCUMENT NUMBER: 1985014870
TITLE: [Inhibitory activity against elastolytic enzymes in bronchial space. On the pathogenesis of chronic airway obstruction].
INHIBITORAKTIVITAT GEGEN ELASTOLYTISCHE ENZYME IM BRONCHIALRAUM. EIN BEITRAG ZUR PATHOGENESE DER CHRONISCHEN ATEMWEGSOBSTRUKTION.
AUTHOR: Rasche B.
CORPORATE SOURCE: Medizinische Abteilung des Silikose-Forschungsinstituts der Bergbau-Berufsgenossenschaft, D-4630 Bochum 1, Germany
SOURCE: Atemwegs- und Lungenkrankheiten, (1984) Vol. 10, No. 8, pp. 389-394.
CODEN: ATLUDF
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: German
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911210
Last Updated on STN: 911210
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L43 ANSWER 71 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 83119909 EMBASE Full-text
DOCUMENT NUMBER: 1983119909
TITLE: Human methionine sulfoxide-peptide reductase, an enzyme

capable of reactivating oxidized alpha-1-proteinase inhibitor in vitro.
AUTHOR: Carp H.; Janoff A.; Abrams W.; et al.
CORPORATE SOURCE: Dep. Pathol., State Univ. New York Stony Brook, Stony Brook, NY 11794, United States
SOURCE: American Review of Respiratory Disease, (1983) Vol. 127, No. 3, pp. 301-305.
CODEN: ARDSBL
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB The present study demonstrates the presence of methionine sulfoxide [Met(O)] peptide reductase activity in human lung homogenates and in lysates of polymorphonuclear leukocytes (PMN) and alveolar type II cells. Enzyme activity was not detected in human bronchoalveolar lavage fluid or in pulmonary alveolar macrophage lysates. The Met(O)-peptide reductase derived from PMN is capable of reactivating alpha-1-proteinase inhibitor (α1Pl) oxidized by treatment with chloramine-T or a myeloperoxidase oxidizing system. However, the PMN-derived enzyme does not reactivate α1Pl inactivated by treatment in vitro with aqueous solutions of cigarette smoke plus peroxide. In addition, after the instillation of oxidized human α1Pl into lungs of normal or ozone-tolerant rats, no reactivated α1Pl could be found in the pulmonary lavage obtained from these animals. Finally, patients with chronic obstructive pulmonary disease appear to have normal levels of PMN Met(O)-peptide reductase.

L43 ANSWER 72 OF 128 EMBASE
ACCESSION NUMBER: 83119904 EMBASE Full-text
DOCUMENT NUMBER: 1983119904
TITLE: Genetic markers in chronic air-flow limitation: A genetic epidemiologic study.
AUTHOR: Kauffmann F.; Kleisbauer J.P.; Cambon De Mouzon A.; et al.
CORPORATE SOURCE: INSERM Unit 169, F-94807 Villejuif Cedex, France
SOURCE: American Review of Respiratory Disease, (1983) Vol. 127, No. 3, pp. 263-269.
CODEN: ARDSBL
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB The distribution of various genetic markers was compared in 2 groups of subjects: never smokers with low FEV1 values (NS-L) and heavy smokers with high FEV1 values (HS-H), for whom the difference in FEV1 values could not be explained by any other known environmental factor. The subjects were men and women 25 to 40 yr of age who had been selected from among 278 never and 777 heavy smokers examined in 1975 in the PAARC survey conducted in the general population of Marseilles and Toulouse, France; 46 in the NS-L and 43 in the HS-H groups were examined in 1980. Alpha1,-antitrypsin, immunoglobulins A, G, M, and E, and haptoglobin studies gave results not different from those expected on the smoking habits data only. The percentage of subjects with low IgD was slightly lower in the HS-H group than in the NS-L group, but the difference was not significant. Genetic systems considered were ABO, Rh, ABH, and Lewis secretor status, protease inhibitor (Pi) haptoglobin (Hp), vitamin D binding protein (DBP), transferrin (Tf), immunoglobulin (Gm and Km), and HLA-A and HLA-B polymorphisms. Results showed a significantly greater increase in ABH nonsecretors belonging to blood group O in NS-L than in HS-H subjects (odds-ratio = 15.6) and a significant decrease in Hp(1S) carriers among non-O blood group subjects in the NS-L group (odds-ratio o.2). We observed a significant increase of the HLA-B7 antigen frequency in the NS-L group compared with that in the HS-H group (odds-ratios, 0.2 and 3.8, respectively). No difference was observed in the Pi system (no subject was PiZ or PiMZ), Gm, Km, Tf, and DBP. Because very few studies allow valid comparisons and our results were obtained on a small sample, our conclusions must be considered only as hypotheses about possible genetic factors involved in chronic air-flow limitation.

L43 ANSWER 73 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 83153655 EMBASE Full-text
DOCUMENT NUMBER: 1983153655
TITLE: Protection of alpha-1 protease inhibitor by plasma antioxidants. Potential abnormality in chronic obstructive pulmonary disease (COPD).
AUTHOR: Taylor J.C.; Oey L.; Mittman C.
CORPORATE SOURCE: Respir. Dis. Dep., City of Hope Med. Cent., Duarte, CA 91010, United States
SOURCE: Chest, (1983) Vol. 83, No. 5 Suppl., pp. 90S-92S.
CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB All normal subjects tested in this study had normal α1Pi levels and phenotypes. The patient population included 6 PiMM, 2 PiMZ and 2 PiZZ individuals. Two of the patients with emphysema had reduced plasma factor activity (approximately 50% of normal). The α1Pi of these patients was identified as PiMM by isoelectric focusing. Their α1Pi levels (functional measurement) were in the normal range. It is possible that an abnormality or deficiency in antioxidant systems in the body may contribute to the pathogenesis of emphysema in some patients, particularly in those individuals with normal levels of serum and lung protease inhibitors.

L43 ANSWER 74 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 83017802 EMBASE Full-text
DOCUMENT NUMBER: 1983017802
TITLE: Effect of corticosteroids on sputum sol-phase protease inhibitors in chronic obstructive pulmonary disease.
AUTHOR: Wiggins J.; Elliott J.A.; Stevenson R.D.; Stockley R.A.
CORPORATE SOURCE: Gen. Hosp., Birmingham B4 6NH, United Kingdom
SOURCE: Thorax, (1982) Vol. 37, No. 9, pp. 652-656.
CODEN: THORA7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB Corticosteroids caused a reduction in the ratio of sol-phase sputum concentration to serum concentration of albumin in 12 patients with chronic obstructive bronchitis, suggesting a reduction in protein transudation. Alpha-1-antitrypsin values followed the same pattern as those of albumin in both the control and treatment periods, confirming the similar behaviour of the two proteins. The α1-antichymotrypsin ratios were on average three times higher than those of albumin in the control period, confirming the presence of local mechanisms in the lung for preferentially concentrating this protein. The sputum-to-serum ratios of α1-antichymotrypsin, however, rose during steroid treatment with the result that there was a selective increase in this protease inhibitor, which may be of potential benefit to such patients.

L43 ANSWER 75 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 82232797 EMBASE Full-text
DOCUMENT NUMBER: 1982232797
TITLE: Ceruloplasmin: Plasma inhibitor of the oxidative inactivation of alpha1-protease inhibitor
AUTHOR: Taylor J.C.; Oey L.
CORPORATE SOURCE: Respir. Dis. Dep., City Hope Med. Cent., Duarte, CA 91010,

United States
SOURCE: American Review of Respiratory Disease, (1982) Vol. 126, No. 3, pp. 476-482.
CODEN: ARDSBL
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB When leukocyte lysosomal extracts are used as a source of elastase and are combined with a fraction of plasma containing sufficient alpha1- protease inhibitor(α1-Pi) to inhibit all but 30 to 40% of the elastase amidase activity, elastolysis occurs at 69% of the rate of the uninhibited elastase controls (0.125 M NaCl; pH, 6.5). Proteolysis of elastin requires the presence of NaCl. At pH 8.6, elastolysis is decreased to 30 to 40% of free elastase controls by 1.0 M NaCl. At pH 6.5, on the other hand, elastolysis is increased to 83% of the control values by these higher NaCl concentrations. The activity of human leukocyte myeloperoxidase is optimal at pH 6 to 6.5 and at NaCl concentrations between 0.25 and 1.0 M. Purified myeloperoxidase, α1-Pi, and elastase, in the presence of NaCl and hydrogen peroxide, can reproduce this phenomenon at pH 6.5, suggesting that the occurrence of elastolysis in lysosomal extract-plasma mixtures may in part be a result of the oxidative inactivation of α1-Pi by myeloperoxidase present in the lysosomal extract. Human ceruloplasmin, the major antioxidant of plasma, inhibits this myeloperoxidase-dependent reaction, without interfering either with free elastase activity or with the appearance of activity in plasma-lysosomal extract mixtures at pH 8.6. The 'antioxidant' activity of ceruloplasmin is inhibited by azide. These results suggest that antioxidants such as ceruloplasmin may be an important determinant of lung defense in persons chronically exposed to oxidants.

L43 ANSWER 76 OF 128 MEDLINE on STN
ACCESSION NUMBER: 83040686 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6291123
TITLE: Serum protease inhibitory capacity. (Recent knowledge on alpha 1-antitrypsin deficiency).
AUTHOR: Massi G; Bruscalupi G; Auconi P
SOURCE: La Ricerca in clinica e in laboratorio, (1982 Jul-Sep) 12 (3) 449-58.
Journal code: 7613947. ISSN: 0390-5748.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198212
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 20000303
Entered Medline: 19821216

AB The molecular structure and the serum levels of alpha 1-antitrypsin, the major antiprotease of human serum, are controlled by a series of codominant alleles at a single chromosomal locus, known as the Pi(protease-inhibitor) locus. The congenital deficiency of this inhibitor is known to be associated with the development of lung emphysema in early adulthood and chronic liver disease in childhood. Less frequent associations have been reported, such as rheumatoid arthritis, membranoproliferative glomerulonephritis and mosaicism for sex chromosomes. The identification of several suballeles of the Pi system, which was accomplished by means of a refinement of the isoelectric focusing technique, has promoted research concerning their possible pathogenic implications. The studies so far performed have often led to contradictory results, but nevertheless they strongly ascribe the property of controlling the quantitative levels of alpha 1-antitrypsin to certain M subtypes. Intermediate M3 subtype has recently been associated with the development of chronic obstructive lung disease in adulthood. Should this finding be confirmed by further evidence, a new approach to the prevention of lung disease could be considered, given that 30% of the individuals are carriers of the M3 suballele. In Italy, the incidence of congenital deficiency of alpha 1-trypsin appears to be greater in the northern regions, where 15-20 out of every 100,000 individuals are affected by the severe (ZZ) form of the deficiency.

L43 ANSWER 77 OF 128 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 1982:558624 CAPLUS Full-text
DOCUMENT NUMBER: 97:158624

TITLE: The isolation of alpha-1-protease inhibitor by a unique procedure designed for industrial application
AUTHOR(S): Glaser, Charles B.; Chamorro, Mario; Crowley, Robert; Karic, Lucy; Childs, Anne; Calderon, Minerva
CORPORATE SOURCE: Inst. Med. Sci., San Francisco, CA, 94115, USA
SOURCE: Analytical Biochemistry (1982), 124(2), 364-71
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A unique, facile 1- or 2-step method is presented for the large-scale isolation of α1-antitrypsin (α1PI) for potential therapeutic use in the treatment of chronic obstructive lung disease. The method takes advantage of the unusual SS bond in α1PI, which consists of a single cysteine residue in the polypeptide chain bound to a free pendant cysteine. In contrast to other circulating plasma proteins, the SS bridge in α1PI does not add to its structural stability. Therefore, if an α1PI-containing solution of plasma proteins is precipitated out in the presence of reductant, much more extensive separation of contaminating proteins will be achieved than in the absence of such reductant. Cohn fraction IV-1, a relatively unused side product in albumin and γ-globulin production, is used as a starting material. After activation of the α1PI in basic media, partial purification is achieved with successive addition of Aerosil (a fumed silica), dithiothreitol, and (NH4)2SO4. From 90 to 95% of the contaminating proteins are precipitated by this single procedure, resulting in a product that is .apprx.70% pure. DEAE-cellulose chromatog. can be used as an addnl. purification step, resulting in a product that is nearly homogeneous. Overall yield is .apprx.45%. The method is simple, inexpensive, and reproducible and is directly applicable to large-scale industrial processing.

L43 ANSWER 78 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 82166132 EMBASE Full-text
DOCUMENT NUMBER: 1982166132
TITLE: [Genetic defects of α1-antitrypsin].
GENETIK DER α1-ANTITRYPSIN-DEFEKTE.
AUTHOR: Cleve H.
CORPORATE SOURCE: Inst. Anthropol. Hum. Genet., Univ. Munchen, D-8000 Munchen, Germany
SOURCE: Wiener Klinische Wochenschrift, (1982) Vol. 94, No. 12, pp. 306-309.
CODEN: WKWOAO
COUNTRY: Austria
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: German
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB A brief review of the protease inhibitor system (Pi) and inherited defects of the plasma protein α1-antitrypsin is presented. The Pi system comprises more than 30 alleles and isoelectrofocusing on polyacrylamide gels is employed for their classification. The defect variant PiZ is associated with disease states: in adults, chronic obstructive pulmonary disease may develop, whilst infants frequently suffer from infantile hepatopathy.

L43 ANSWER 79 OF 128 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 11
ACCESSION NUMBER: 1982:216250 SCISEARCH Full-text
THE GENUINE ARTICLE: NM406
TITLE: THE EFFECT OF STEROIDS ON SPUTUM PROTEASE INHIBITORS AND LEUKOCYTE ELASTASE IN CHRONIC OBSTRUCTIVE LUNG-DISEASE
AUTHOR: ELLIOTT J A (Reprint); WIGGINS J; STEVENSON R D; DORWARD A J; STOCKLEY R A
CORPORATE SOURCE: WESTERN INFIRM, DEPT RESP MED, GLASGOW G11 6NT, SCOTLAND (Reprint); GEN HOSP, BIRMINGHAM B4 6NH, W MIDLANDS,

ENGLAND; GLASGOW ROYAL INFIRM, CTR RESP INVEST, GLASGOW G4 0SF, SCOTLAND
COUNTRY OF AUTHOR: SCOTLAND; ENGLAND
SOURCE: SCOTTISH MEDICAL JOURNAL, (1982) Vol. 27, No. 2, pp. 191-191.
ISSN: 0036-9330.
PUBLISHER: HERMISTON PUBLICATIONS LTD, 9 STONELAWS WHITEKIRK, EAST LOTHIAN EH40 3DX, SCOTLAND.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

L43 ANSWER 80 OF 128 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 82249178 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6980436
TITLE: Alpha 1-antitrypsin genetic phenotypes in a group of children suffering from pulmonary diseases.
AUTHOR: Petrovic J; Trajkovic D; Radojcic M; Matic G; Milovanov N; Todorovic O
SOURCE: Respiration; international review of thoracic diseases, (1982) 43 (2) 127-31.
Journal code: 0137356. ISSN: 0025-7931.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198209
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19900317
Entered Medline: 19820924
AB Alpha 1-antitrypsin (AAT), the main protease inhibitor of human sera, was studied in a group of 88 children suffering from different pulmonary diseases, with the hope that some of the potential victims of chronic obstructive lung diseases can be identified in time. AAT genetic phenotypes were determined using acid agarose gel electrophoresis, followed by crossed antigen-antibody electrophoresis in agarose gel. Identification of the banding patterns revealed 10.2% of AAT variants. 4.54% of the patients were MZ, 3.40% were MS and 89.77% were MM. During this study, 1 FF and 1 MV subject were also found. All AAT variants were in the group of younger children, under 6 years of age.

L43 ANSWER 81 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 82176920 EMBASE Full-text
DOCUMENT NUMBER: 1982176920
TITLE: COPD and endobronchial polyposis associated with hypogammaglobulinemia. Are proteolytic enzymes involved?.
AUTHOR: Fein A.M.; Lipschutz J.B.; Lee C.T.; et al.
CORPORATE SOURCE: Albert Einstein Med. Cent., Philadelphia, PA 19141, United States
SOURCE: Chest, (1982) Vol. 82, No. 1, pp. 127-129.
CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209
AB The present report describes a patient who had severe obstructive lung disease in association with acquired hypogammaglobulinemia. Evidence obtained by bronchoalveolar lavage is presented that suggest that his lung disease resulted from both a marked increase in elastase load and a reduction in protease inhibitor function.

L43 ANSWER 82 OF 128 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 81121111 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6257988
TITLE: Heterozygous defects in alpha 1-antitrypsin and low-density lipoprotein receptor. Simultaneous occurrence in a

pediatric patient.
AUTHOR: Cornicelli J A; Weidman W H; Gilman S R; Krom B A; Kottke B A
CONTRACT NUMBER: HL-07329 (NHLBI)
HL-23465 (NHLBI)
SOURCE: Mayo Clinic proceedings, (1981 Feb) 56 (2) 113-6.
Journal code: 0405543. ISSN: 0025-6196.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198104
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19970203
Entered Medline: 19810413

AB alpha 1-Antitrypsin is a serum protein protease inhibitor. The homozygous deficiency state for alpha 1-antitrypsin is associated with the development of chronic obstructive lung disease and liver cirrhosis. Familial hypercholesterolemia is a genetic defect in which the nonhepatic tissues of affected persons are partially or completely deficient in cellular receptors for low-density lipoproteins, the major plasma cholesterol transport protein. Homozygotes and heterozygotes for familial hypercholesterolemia experience premature coronary artery disease. We have identified a young patient who manifested heterozygous deficiencies for both of these gene products. The occurrence of these defects in tandem has not been previously reported.

L43 ANSWER 83 OF 128 EMBASE
ACCESSION NUMBER: 81136680 EMBASE Full-text
DOCUMENT NUMBER: 1981136680
TITLE: Ultrasonic method of sputum homogenization and its application in the study of the enzymic content of sputum.
AUTHOR: Girard F.; Tournier J.M.; Polu J.M.; et al.
CORPORATE SOURCE: Unite Physiopathol. Respirat., INSERM U-14, 54500 Vandoeuvre-Les-Nancy, France
SOURCE: Clinica Chimica Acta, (1981) Vol. 113, No. 1, pp. 105-109.
CODEN: CCATAR
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
015 Chest Diseases, Thoracic Surgery and Tuberculosis
027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB The aim of this project was to perfect a homogenization method, based solely on ultrasound, and to define experimental conditions such that the enzymic activities (trypsin-like, chymotrypsin-like, elastase, collagenase) and the integrity of the cells (leukocytes and bacteria) would be preserved.

L43 ANSWER 84 OF 128 EMBASE
ACCESSION NUMBER: 81124842 EMBASE Full-text
DOCUMENT NUMBER: 1981124842
TITLE: **Protease inhibitor** phenotypes and pulmonary disease in patients with Sjogren's syndrome.
AUTHOR: Karsh J.; Moutsopoulos H.M.; Vergalla J.; Jones E.A.
CORPORATE SOURCE: Clin. Immunol. Sect., Nat. Inst. Dent. Res., NIH, Bethesda, Md. 20205, United States
SOURCE: Respiration, (1981) Vol. 41, No. 1, pp. 60-65.
CODEN: RESPBD
COUNTRY: Switzerland
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
031 Arthritis and Rheumatism
026 Immunology, Serology and Transplantation
012 Ophthalmology
LANGUAGE: English

ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB The incidence of pulmonary emphysema in patients with alpha-1-antitrypsin (α-1-AT) deficiency associated with the protease inhibitor (Pi) phenotype ZZ is increased. To determine whether less severe deficiency states of α-1-AT (i.e. Pi phenotypes other than ZZ and MM) might predispose to the development of pulmonary disease, Pi phenotypes were determined in a group of patients in whom the incidence of chronic pulmonary disease is high. The proportion of 52 patients with Sjogren's syndrome who had Pi phenotypes other than ZZ and MM was not significantly greater than that for populations of normal subjects. Mean values for tests of pulmonary function, including estimates of both restrictive lung disease and airway obstruction in patients with the MM phenotype were not significantly different from corresponding means for patients with non-MM phenotypes. These findings suggest that the increased susceptibility of patients with Sjogren's syndrome to develop chronic obstructive pulmonary disease is not attributable to an abnormally high frequency of non-MM phenotypes and associated moderately reduced serum levels of α-1-AT.

L43 ANSWER 85 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 81110166 EMBASE Full-text
DOCUMENT NUMBER: 1981110166
TITLE: Familial aggregation of abnormal ventilatory control and pulmonary function in chronic obstructive pulmonary disease.
AUTHOR: Kawakami Y.; Irie T.; Kishi F.; et al.
CORPORATE SOURCE: I Dept. Med., Sch. Med., Hokkaido Univ., Sapporo 060, Japan
SOURCE: European Journal of Respiratory Diseases, (1981) Vol. 62, No. 1, pp. 56-64.
CODEN: EJRDD2
COUNTRY: Denmark
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: French
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB A sex-, obesity-, and protease inhibitor-matched study of pulmonary function and ventilatory control was performed on 26 sons of 19 patients with chronic obstructive pulmonary disease (COPD) and 26 control subjects. Mean values for FEV1/FVC and V25 were significantly lower and CV/VC was significantly higher in sons of patients than in the controls. VC, airway resistance, static pulmonary compliance, ΔN2, arterial blood gases and pH were not different between sons and controls. When the sons of patients were divided into two groups according to the arterial blood gases of their parents, sons of hypoxemic, hypercapnic parents showed significantly lower hypoxic ventilatory responses than sons of normoxemic, normocapnic parents. Hypercapnic ventilatory responses were not different between sons and controls. Abnormal pulmonary function and low ventilatory responses were more frequently detected in sons than in controls. The association of smoking with abnormalities of pulmonary function was not clearly seen in sons. These results suggest that familial factors (either genetic or environmental) play a significant role in determining the pathogenesis and clinical types of COPD.

L43 ANSWER 86 OF 128 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1981:47635 BIOSIS Full-text
DOCUMENT NUMBER: PREV198120047635; BR20:47635
TITLE: GENETIC FACTORS IN CHRONIC OBSTRUCTIVE LUNG DISEASE.
AUTHOR(S): MENKES H A [Reprint author]; COHEN B H; LEVY D A; KREISS P; PERMUTT S; TIELSH J
CORPORATE SOURCE: DEP OF ENVIRONMENTAL HEALTH SCIENCES, DIV OF ENVIRONMENTAL PHYSIOL, JOHNS HOPKINS UNIV SCH OF HYGIENE AND PUBLIC HEALTH, 615 N WOLFE STREET, BALTIMORE, MD 21205, USA
SOURCE: Clinical Respiratory Physiology, (1980) Vol. 16, No. SUPPL, pp. 357-366.
Meeting Info.: INTERNATIONAL SYMPOSIUM ON BIOCHEMISTRY, PATHOLOGY AND GENETICS OF PULMONARY EMPHYSEMA, PORTO CONTE, SASSARI, ITALY, APRIL 27-30, 1980. CLIN RESPIR PHYSIOL.
CODEN: CRPHD4. ISSN: 0272-7587.

DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH

L43 ANSWER 87 OF 128 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 14
ACCESSION NUMBER: 1981:53739 BIOSIS Full-text
DOCUMENT NUMBER: PREV198120053739; BR20:53739
TITLE: INACTIVATION OF ALPHA-1 PROTEINASE INHIBITOR AND BRONCHIAL MUCOUS PROTEINASE INHIBITOR BY CIGARETTE SMOKE IN-VITRO AND IN-VIVO.
AUTHOR(S): JANOFF A [Reprint author]; CARP H; LEE D K
CORPORATE SOURCE: DEP OF PATHOL, HEALTH SCIENCES CENTER, STATE UNIV OF NEW YORK, STONY BROOK, NY 11794, USA
SOURCE: Clinical Respiratory Physiology, (1980) Vol. 16, No. SUPPL, pp. 321-340.
Meeting Info.: INTERNATIONAL SYMPOSIUM ON BIOCHEMISTRY, PATHOLOGY AND GENETICS OF PULMONARY EMPHYSEMA, PORTO CONTE, SASSARI, ITALY, APRIL 27-30, 1980. CLIN RESPIR PHYSIOL.
CODEN: CRPHD4. ISSN: 0272-7587.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH

L43 ANSWER 88 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 80247318 EMBASE Full-text
DOCUMENT NUMBER: 1980247318
TITLE: A family with abnormal ventilatory control and pulmonary functions.
AUTHOR: Kawakami Y.; Irie T.; Asanuma Y.; et al.
CORPORATE SOURCE: I Dept. Med., Sch. Med., Hokkaido Univ., Sapporo, Japan
SOURCE: Japanese Journal of Thoracic Diseases, (1980) Vol. 18, No. 5, pp. 304-310.
CODEN: NKYZA2
COUNTRY: Japan
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
LANGUAGE: Japanese
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209
AB Six family members (wife, 3 sons and 2 daughters) of a patient with pulmonary emphysema and chronic bronchitis were studied for ventilatory response against hypoxia and hypercapnia, pulmonary functions and serum protease inhibitors. Ventilatory response against hypoxia was abnormally low in 2 sons and 2 daughters. One son showed a low ventilatory response against hypercapnia. The pulmonary functions of the wife were abnormal in FEV1/FVC, Raw, PaO2, D[LCO], CV/VC, ΔN2, V.ovrhdot.50 and V.ovrhdot.25. Three sons and 1 daughter showed abnormal pulmonary functions. Serum protease inhibitors (a1-antitrypsin, a2-macroglobulin, C1-inactivator, antithrombin III, and a2-plasmin inhibitor) were within normal limits in all the family members. These results suggest involvement of familial factors in ventilatory control and pulmonary function.

L43 ANSWER 89 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 81156067 EMBASE Full-text
DOCUMENT NUMBER: 1981156067
TITLE: Inactivation of bronchial mucous proteinase inhibitor by cigarette smoke and phagocyte-derived oxidants.
AUTHOR: Carp H.; Janoff A.
CORPORATE SOURCE: Dept. Pathol., Hlth Sci. Cent., State Univ. New York, Stony Brook, N.Y. 11794, United States
SOURCE: Experimental Lung Research, (1980) Vol. 1, No. 3, pp. 225-237.
CODEN: EXLRDA
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index

015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
030 Pharmacology
026 Immunology, Serology and Transplantation

LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB Freshly prepared aqueous solutions of cigarette smoke suppressed the elastase inhibitory capacity (EIC) of the acid-stable proteinase inhibitor present in bronchial mucus (BMPi) and human seminal plasma (HUSI-I). Thin-layer gel-immunofiltration analysis of mixtures of smoke-treated BMPi and human leukocyte elastase showed decreased elastase: BMPi complexes, increased uncomplexed BMPi and increased free elastase. Phenolic antioxidants prevented the suppression of the EIC of BMPi or HUSI-I by cigarette smoke. In addition, treatment of BMPi or HUSI-I with chemical oxidants caused a similar suppression of EIC. Furthermore, treatment of BMPi or HUSI-I with the phagocyte-derived oxidizing system, myeloperoxidase + H2O2 + Cl-, suppressed EIC. Finally, the functional activity of BMPi was significantly reduced in tracheal aspirates of human smokers compared to that of nonsmokers. These results support the hypothesis that local inactivation of BMPi in the conducting airways of the lung by inhaled cigarette smoke or by phagocyte-derived oxidants may play a role in the pathogenesis of obstruction lung disease in smokers.

L43 ANSWER 90 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 80094215 EMBASE Full-text
DOCUMENT NUMBER: 1980094215
TITLE: Patterns of forced expiratory flows in groups at risk for chronic obstructive pulmonary disease.
AUTHOR: Graves C.G.; Menkes H.A.; Chase G.A.; et al.
CORPORATE SOURCE: Dept. Epidemiol., Johns Hopkins Univ. Sch. Hyg. Publ. Hlth, Baltimore, Md. 21205, United States
SOURCE: Johns Hopkins Medical Journal, (1980) Vol. 146, No. 2, pp. 41-48.
CODEN: JHMJAX
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
006 Internal Medicine
LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB In a modified case-control study of chronic obstructive pulmonary disease (COPD), airways obstruction has been found to be associated with age, sex, protease inhibitor type, socioeconomic status (SES) and smoking. In this paper patterns of forced expiratory flows are examined in persons demonstrating various risk factors. Two broad patterns of flow limitation emerge. The first pattern, characterized by lower flows at high lung volumes, is found in first-degree relatives of patients with COPD and subjects with a low SES. This pattern, consistent with dysfunction of large airways, may reflect reversible decreases of airway caliber. The second pattern, characterized by lower flows at low lung volumes, is found in older subjects. This pattern, consistent with nonhomogenously emptying lungs or dysfunction of small airways, may reflect more chronic irreversible changes. Smokers and male subjects exhibit both patterns of flow limitation when compared with subjects who had never smoked and female subjects. It is possible that the combination of the patterns reflects a particularly high risk for the development of COPD in male smokers.

L43 ANSWER 91 OF 128 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 15

ACCESSION NUMBER: 1980:213668 BIOSIS Full-text
DOCUMENT NUMBER: PREV198070006164; BA70:6164
TITLE: THE IMPORTANCE OF PROTEASE INHIBITORS FOR THE LOCAL DEFENSE MECHANISM OF THE LUNG.
AUTHOR(S): RASCHE B [Reprint author]
CORPORATE SOURCE: BIOL ABT, SILIKOSE-FORSCHUNGSINST BERGBAU BG, HUNSCHEIDSTR 12, D-4630 BOCHUM, W GER
SOURCE: Atemwegs-und Lungenkrankheiten, (1980) Vol. 6, No. 1, pp. 5-8.
CODEN: ATLUDF. ISSN: 0341-3055.
DOCUMENT TYPE: Article
FILE SEGMENT: BA

LANGUAGE: GERMAN

AB In patients with chronic obstructive lung diseases an augmented number of proteases in the bronchial area are released. These proteases originated primarily from decomposing polymorphonuclear leukocytes. Proteases interfere with the immunological system, contribute to a histamine release by mastocytes and induce bronchoconstriction. In bronchial secretions there were protease inhibitors capable of inhibiting leukocyte proteases. These inhibitors are measurable in the sputum.

L43 ANSWER 92 OF 128 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:89904 CAPLUS Full-text
DOCUMENT NUMBER: 92:89904
TITLE: Characterization of the cytoplasmic proteinase inhibitor of horse leukocytes with fibrinogen plate electrophoresis: migration and enzyme and organ specificity
AUTHOR(S): Von Fellenberg, R.; Pellegrini, A.
CORPORATE SOURCE: Inst. Vet.-Physiol., Univ. Zurich, Zurich, CH-8057, Switz.
SOURCE: Schweizer Archiv fuer Tierheilkunde (1979), 121(11), 593-601
CODEN: SATHAA; ISSN: 0036-7281
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The proteinase inhibitor of horse leukocytes was analyzed by fibrinogen plate electrophoresis. The inhibitor migrated to the β-region and could easily be distinguished from the serum inhibitors. Its enzyme specificity was poor, and it inhibited the pancreatic enzymes trypsin, chymotrypsin, and elastase as well as all neutral leukocyte proteinases. The inhibitor was detected in small amts. in the cytoplasmic fraction of the lung but not of the liver. The importance of the inhibitor as a possible pathogenic factor for chronic-obstructive lung disease is discussed.

L43 ANSWER 93 OF 128 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 79219712 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 313477
TITLE: [Clinical-functional emphysema diagnostics and immunological correlations (author's transl)]. Klinisch-funktionelle Emphysemdiagnostik und immunologische Korrelationen.
AUTHOR: Kowalski J; Rasche B; Bulgalho de Almeida A A; Hochstrasser K; Ulmer W T
SOURCE: Klinische Wochenschrift, (1979 May 16) 57 (10) 521-7.
Journal code: 2985205R. ISSN: 0023-2173.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197909
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19790917

AB By application of the correlation flow resistance/intrathoracic gas volume the lung emphysema is differentiated in quality within the scope of chronic obstructive lung diseases. For these groups immunoglobulins, the alpha1-trypsin activity in serum and the activity of further protease inhibitors were determined. There are no substantial variables in the different groups with regard to immunoglobulins. In the emphysema group alpha1-antitrypsin was a little reduced. This group included 2 patients with an alpha1-antitrypsin deficit. The two-dimensional separation of the inter-alpha-trypsin big inhibitor shows 3 areas which decrease significantly in case of severe emphysemata. The irritation of the inter-alpha-trypsin big inhibitor, i.e. in its turnover, parallel to the increasing degree of emphysema formation, is discussed.

L43 ANSWER 94 OF 128 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 80014450 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 482922
TITLE: [Protease inhibitors from lung, secretions and blood in horses and cattle: a comparative study on endogenous, predisposing factors of chronic obstructive lung

disease].
Lungen-, Sekret- und Blutproteaseinhibitoren von Pferd und Rind: Eine vergleichende Studie uber endogene, pradisponierende Faktoren fur chronisch-obstruktive Lungenkrankheiten.
AUTHOR: von Fellenberg R; Minder H; Wegmann C; Frei F
SOURCE: Schweizer Archiv fur Tierheilkunde, (1979 Jul) 121 (7) 355-65.
Journal code: 0424247. ISSN: 0036-7281.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197911
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19791129

L43 ANSWER 95 OF 128 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 80103213 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 316573
TITLE: Alpha 1-antitrypsin phenotypes and obstructive lung disease in the city of Oslo.
AUTHOR: Gulsvik A; Fagerhol M K
SOURCE: Scandinavian journal of respiratory diseases, (1979 Oct) 60 (5) 267-74.
Journal code: 0055427. ISSN: 0036-5572.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198003
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19970203
Entered Medline: 19800327

AB In a community survey in Oslo, Norway, comprising 1268 persons, alpha 1-antitrypsin concentration in serum (AT) and protease- inhibitor (Pi) phenotypes were examined in 1258 subjects. Estimated percentage distribution of Pi-phenotypes in the target population aged 15--70 years was M 87.30%, MS 4.65%, MZ 4.73%, FM 2.69%, SZ 0.13%, IM 0.20%, FZ 0.07%, S 0.06%, FS 0.07% and Z 0.06%. The distribution curve of AT had a normal (Gaussian) shape and the ranges of AT demonstrated great overlap of types MS and MZ with type M. In subjects with phenotype MZ neither respiratory symptoms nor physicians' diagnoses of chronic obstructive lung disease (COLD) were more frequent than in M subjects. Physicians' diagnoses of COLD were slightly more frequent (0.06 greater than P greater than 0.01) in subjects with phenotype MS than M, probably due to there being more smokers in the MS group. Spirometric variables given as per-cent of predicted values yielded large differences between smokers and non-smokers but no differences among phenotypes M, MS and MZ. Radiologic signs of hypertransradiancy and/or emphysema were evently distributed in M, MS and MZ subjects. The only subject observed with Pi-type Z and one out of three subjects with type SZ had COLD. In neither smokers nor non-smokers is phenotype MZ a risk factor of clinical importance for development of obstructive lung disease.

L43 ANSWER 96 OF 128 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1980:203230 BIOSIS Full-text
DOCUMENT NUMBER: PREV198069078226; BA69:78226
TITLE: SEGREGATION OF THE PI ALLELES M-1 M-2 F AND Z IN A LARGE PEDIGREE.
AUTHOR(S): BECKMAN G [Reprint author]; MIKAELSSON B; RUDOLPHI O; STJERNBERG N; THUNELL M; WIMAN L-G
CORPORATE SOURCE: DEP MED GENET, UNIV UMEA, S-901 87 UMEA, SWED
SOURCE: Hereditas (Lund), (1979) Vol. 91, No. 2, pp. 241-244.
CODEN: HEREAY. ISSN: 0018-0661.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB A large pedigree is reported in which the Pi [protease inhibitor; α1-antitrypsin] alleles Z, F, M1 and M2 were segregating. The Z gene [associated with pathological manifestations such as childhood liver cirrhosis and chronic obstructive lung disease] entered the

pedigree 4 times in spite of the fact that no close inbreeding was found. Serum levels of α1-antitrypsin and some data on lung disease are presented.

L43 ANSWER 97 OF 128 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 79207526 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 313173
TITLE: Protease inhibitor variants in children and young adults with chronic asthma.
AUTHOR: Hyde J S; Werner P; Kumar C M; Moore B S
SOURCE: Annals of allergy, (1979 Jul) 43 (1) 8-13.
Journal code: 0372346. ISSN: 0003-4738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197908
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19790829

AB The results of systematic medical histories and pulmonary function tests on 26 children and young adults, 10 with Pi variant alpha1-antitrypsin phenotypes and 16 Pi normals, are reported. These subjects were selected from 57 consecutive patients who had chronic asthma. The incidence of Pi variants was 20.4% among 46 Caucasian subjects (ages seven to 21 years). The Pi variant patients required more bronchodilators and long-term corticosteroid therapy. Among the parents and siblings, 50% of those with abnormal Pi type had chronic obstructive lung disease. Grandparents of the Pi abnormal probands had greater incidence of chronic obstructive lung disease (P less than 0.05). Baseline specific airways conductance and maximal midexpiratory flow rates did not discriminat between the two groups. However, bronchodilator inhalation showed the Pi variant group to be significantly less responsive than the Pi normal group. Pi heterozygous state, particularly Pi MZ, should be considered when a young person with chronic asthma is unresponsive to adequate doses of bronchodilators and needs prolonged use of corticosteroids.

L43 ANSWER 98 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 79091320 EMBASE Full-text
DOCUMENT NUMBER: 1979091320
TITLE: Protease inhibitor profile of black Americans with and without chronic cardiopulmonary disease.
AUTHOR: Young Jr. R.C.; Headings V.E.; Henderson A.L.; et al.
CORPORATE SOURCE: Harden Pulmon. Lab., Pulmon. Dis. Div., Howard Univ. Hosp., Washington, D.C. 20060, United States
SOURCE: Journal of the National Medical Association, (1978) Vol. 70, No. 11, pp. 849-856.
CODEN: JNMAAE
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
017 Public Health, Social Medicine and Epidemiology
LANGUAGE: English

AB An epidemiologic study of protease inhibitor (alpha1-antitrypsin) was undertaken among 599 ambulatory and hospitalized black American patients with chronic cardiopulmonary disease referred for pulmonary function testing, and 115 ethnically matched, healthy control subjects. Clinical evaluation consisted of respiratory questionnaire completion, physical examination, chest radiograph, and spirography. Protease inhibitor evaluation consisted of measurement of serum trypsin inhibitory capacity in all subjects corrected by comparison with control sera, while 200 of these subjects were phenotyped for alpha1-antitrypsin electrophoretic variants. Results showed mean serum trypsin inhibitory capacity for all subjects was 1.56, SD ± 0.47 mg/ml, while corrected values were 111.2, SD ± 30.5 percent of control. Acute phase reactivity was present for patients with heart disease, pulmonary malignancy, $p<0.01$ for both, and pulmonary fibrosis, $p<0.05$, when compared with controls. Prevalence of protease inhibitor variants in 29 controls was two heterozygotes for the Z variant (seven percent), and one homozygote for the S variant. Among 94 patients with chronic obstructive pulmonary disease, prevalence was 1.1 percent each for ZZ sand SZ phenotypes, and 2.1 percent for MZ. Surprisingly, the sole ZZ patient had asthmatic bronchitis rather than emphysema. Computed allele frequencies for Pi M and Z were comparable to those for a random sample of black Americans in St. Louis, but differed from a sample of black infants in Brooklyn, NY. These results indicate that protease

inhibitor deficiency variants are not as uncommon among black Americans as the literature suggests. Furthermore, the heterozygous state is not necessarily a risk factor in development of chronic obstructive pulmonary disease. Protease inhibitor deficiency states therefore appear to play less important a role in etiology of chronic cardiopulmonary disease in black Americans than among their Caucasian counterparts.

L43 ANSWER 99 OF 128 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1979:135633 CAPLUS Full-text
DOCUMENT NUMBER: 90:135633
TITLE: Electrophoretic analysis of protease inhibitors in horses serum
AUTHOR(S): Von Fellenberg, R.
CORPORATE SOURCE: Inst. Veterinaerphysiol., Univ. Zurich, Zurich, Switz.
SOURCE: Schweizer Archiv fuer Tierheilkunde (1978), 120(12), 631-42
CODEN: SATHAA; ISSN: 0036-7281
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Inhibitors for chymotrypsin, trypsin, elastase, and plasmin were studied in 18 horses with fibrinogen plate electrophoresis. Plasmin was mainly inhibited by α2-macroglobulin (α2M). Besides α2M, an anodically migrating group of inhibitors in the albumin-prealbumin region was responsible for inhibition of chymotrypsin, trypsin, and elastase. These inhibitors were heterogeneous. Three inhibitors for chymotrypsin, 3 for trypsin, and ≥2 for elastase were identified. Not more than 2 inhibitors for 1 enzyme were present in the serum of a single animal. The banding patterns showed individual differences. Four patterns for chymotrypsin and 3 for trypsin could be distinguished in the 18 horses studied. Elastase inhibitors showed fewer individual differences. This may partly be due to the low resolving power of the method used. The possible implications of the heterogeneity of the inhibitors for the pathogenesis of chronic obstructive lung diseases are discussed.

L43 ANSWER 100 OF 128 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 78207764 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 78661
TITLE: Proteases and protease inhibitors in chronic obstructive lung disease.
AUTHOR: Erikson S
SOURCE: Acta medica Scandinavica, (1978) 203 (6) 449-55.
Journal code: 0370330. ISSN: 0001-6101.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197808
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19780814

L43 ANSWER 101 OF 128 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:560655 CAPLUS Full-text
DOCUMENT NUMBER: 89:160655
TITLE: A comparative study of trypsin inhibitors in lung tissue and serum of horses and cattle
AUTHOR(S): Von Fellenberg, R.
CORPORATE SOURCE: Inst. Vet.-Physiol., Univ. Zurich, Zurich, Switz.
SOURCE: Schweizer Archiv fuer Tierheilkunde (1978), 120(7), 343-55
CODEN: SATHAA; ISSN: 0036-7281
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The incidence of chronic alveolar emphysema and bronchiolitis is known to be very high in the horse, but virtually absent in cattle. In the present study, lung tissue of cattle was shown to contain the known tissue inhibitor Trasylol, which is soluble in perchloric acid. A 2nd, acid-labile inhibitor, which may be tissue-specific, was also detected. The lung of the horse lacked any tissue-specific trypsin inhibitors. The trypsin inhibitory capacity of serum was not significantly different between the 2 species. It is still premature to state that the susceptibility of horses to chronic obstructive lung disease is definitely related to the absence of lung trypsin inhibitor, as other protease inhibitors, possibly in the serum, may be involved.

L43 ANSWER 102 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 78346637 EMBASE Full-text
DOCUMENT NUMBER: 1978346637
TITLE: Inter-alpha-trypsin inhibitor in serum and bronchial mucus inhibitor in sputum in chronic airway obstruction.
AUTHOR: Rasche B.; Hochstrasser K.; Ulmer W.T.
CORPORATE SOURCE: Med. Abt. Silikose-Forsch. Inst., Bergbau-Berufsgenossensch, Bochum, Germany
SOURCE: Respiration, (1978) Vol. 36, No. 1, pp. 39-47.
CODEN: RESPBD
COUNTRY: Switzerland
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
030 Pharmacology
006 Internal Medicine
LANGUAGE: English

AB Diseases in the bronchial tract release proteases, mainly from disintegrated leucocytes. These elastase-like enzymes, chiefly from granulocytes, are capable of increasing the bronchial resistance. The feeble, monovalent, humoral protease inhibitor inter-α-trypsin inhibitor (ITI) has to be regarded as a stage for different secretory, low-molecular, polyvalent protease inhibitors, among others for the bronchial mucus inhibitor. Thereby, kallikreins act as inhibitor-releasing enzymes. Patients with a severe, chronic obstructive bronchitis did not show significantly increased serum levels of the proinhibitor ITI, whereas there was measured a high transformation increase of the single, immunologically active derivatives as intermediate stage towards bronchial mucus. The transformation extent depended on the airway resistance; it was highest at a high resistance about R(t) = 10; at a normal or only slightly increased resistance it almost corresponded to the normal value. In the case of purulent sputa the concentrations of the bronchial mucus inhibitor were higher than for mucous sputa, thus showing some correlation between protease appearance and concentration of the bronchial mucus inhibitor. If we suppose that those derivates of ITI which are no longer seen in the serum already develop locally, the enzymatic reduction in the damaged mucosa seems to be inhibited in the case of no or only low concentrations of the bronchial mucus inhibitor. According to our research method, no correlation between ITI in the serum and bronchial mucus inhibitor in the sputum could be found.

L43 ANSWER 103 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 78111848 EMBASE Full-text
DOCUMENT NUMBER: 1978111848
TITLE: Relation of protease inhibitor phenotypes to obstructive lung diseases in a community.
AUTHOR: Morse J.O.; Lebowitz M.D.; Knudson R.J.; Burrows B.
CORPORATE SOURCE: Clin. Chest Sect., VA Hosp., Tucson, Ariz., United States
SOURCE: New England Journal of Medicine, (1977) Vol. 296, No. 21, pp. 1190-1194.
CODEN: NEJMAG
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
006 Internal Medicine
030 Pharmacology
005 General Pathology and Pathological Anatomy
LANGUAGE: English

AB To examine the relative risk for the development of obstructive lung disease in persons heterozygous for alpha1-antitrypsin deficiency, we determined protease inhibitor phenotypes in 2944 subjects in a general community population. Phenotype M was found in 89.5%, MS in 7.1%, and MZ in 3.0% of the population. There were 2 persons of phenotype Z and 6 of phenotype SZ. The study also included respiratory questionnaires and spirometry. There were no statistically significant differences in the prevalence of respiratory symptoms and diagnoses or of ventilatory impairment among the three major phenotype groups (M; MS and MZ), nor were there differences in the rates of deterioration of function with age or smoking. Consequently, we do not consider population screening for heterozygous alpha1-antitrypsin deficiency to be worthwhile.

L43 ANSWER 104 OF 128 MEDLINE on STN DUPLICATE 21
ACCESSION NUMBER: 77226675 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 301850
TITLE: Population genetics of alpha1-antitrypsin in the Netherlands. Description of a new electrophoretic variant.
AUTHOR: Klasen E C; Franken C; Volkers W S; Bernini L F
SOURCE: Human genetics, (1977 Jul 26) 37 (3) 303-13.
Journal code: 7613873. ISSN: 0340-6717.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197709
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19770929
AB Two groups of 708 healthy blood donors and 563 patients affected with chronic obstructive lung disease (C.O.L.D.) respectively, have been screened for alpha1-antitrypsin (alpha1AT) variants by electrophoresis on agarose-polyacrylamide gels at pH 4.7 and isoelectric focusing (IEF). The frequencies of the Pi (Protease inhibitor) alleles are comparable to those observed in the North European populations. As expected, the frequency of the Z gene is higher in the group of patients with C.O.L.D. Also the frequency of MZ phenotypes is higher among these patients, but in this case the difference is not statistically significant. With the aid of the electrophoretic methods described in the text we were able to detect a new electrophoretic variant (M3) showing a mobility intermediate between the M1 and the M2 phenotypes.

L43 ANSWER 105 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 77211836 EMBASE Full-text
DOCUMENT NUMBER: 1977211836
TITLE: [Genetics and chronic obstructive bronchopneumopathies]. GENETIQUE ET BRONCHOPNEUMOPATHIES CHRONIQUES OBSTRUCTIVES. ASPECTS ACTUELS.
AUTHOR: Dyan A.; Bignon J.
CORPORATE SOURCE: Hop. Laennec, Paris, France
SOURCE: Concours Medical, (1976) Vol. 98, No. 46, pp. 7373-7383.
CODEN: COMEAO
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
007 Pediatrics and Pediatric Surgery
LANGUAGE: French
AB At the present time only a few factors are known that are directly responsible for, or predispose to emphysema and to obstructive chronic bronchopneumopathies. Mucoviscidosis is an exceptional genetic factor, at least in the adult. The complete form is observed in the child, combining pancreatic insufficiency and severe bronchopathy. In the young adult mucoviscidosis comes up for discussion only very exceptionally in isolated bronchitic forms. Deficiency of alpha 1 antitrypsin is another genetic factor and is more important in the adult than in the child; its linkage with pulmonary emphysema and the obstructive chronic bronchopneumopathies is described. This deficiency is of hereditary transmission, and a complex protein system (protease inhibitor system Pi) has been demonstrated. There is no doubt that these genetic factors are not the only causes. They certainly come into action in association with environmental factors (tobacco, pollution, bronchial infections and allergens). The practitioner is nowadays better armed for the struggle against these environmental factors, but study of the genetic factors predisposing to obstructive chronic bronchopneumopathies is a much more promising line of research in this wide sector of pneumology than are chronic bronchitis and pulmonary emphysema.

L43 ANSWER 106 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 77079876 EMBASE Full-text
DOCUMENT NUMBER: 1977079876
TITLE: Protease inhibitors in patients with chronic obstructive pulmonary disease: the alpha antitrypsin heterozygote controversy.
AUTHOR: Cox D.W.; Hoeppner V.H.; Levison H.
CORPORATE SOURCE: Res. Inst., Hosp. Sick Child., Toronto, Canada

SOURCE: American Review of Respiratory Disease, (1976) Vol. 113, No. 5, pp. 601-606.
CODEN: ARDSBL
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
015 Chest Diseases, Thoracic Surgery and Tuberculosis
006 Internal Medicine
029 Clinical Biochemistry
026 Immunology, Serology and Transplantation
LANGUAGE: English

AB A group of 163 patients with chronic obstructive pulmonary disease, from the pulmonary service of a large urban hospital, were evaluated for their protease inhibitor (Pi) type by starch gel and crossed immunoelectrophoresis, for serum concentrations of α1 antitrypsin and α1 antichymotrypsin, and for pulmonary function. Of the patients with emphysema, 17.8 percent were of Pi type Z; 50 percent of these were less than 45 years of age, compared to 13 percent of those of Pi type M. Of all patients with chronic obstructive pulmonary disease, 4.9 percent were of Pi type Z; 4.9 percent of patients were of Pi type MZ (heterozygotes) compared with 1.9 percent of the control population. There was an increased incidence of chronic obstructive pulmonary disease in persons of Pi type MZ, but no increase in persons of Pi type MS. Concentrations of both α1 antitrypsin and α1 antichymotrypsin were increased and were correlated. No patient had a deficiency of α1 antichymotrypsin.

L43 ANSWER 107 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 77163792 EMBASE Full-text
DOCUMENT NUMBER: 1977163792
TITLE: A new method for the determination of α1 protease inhibitor (α1 antitrypsin) phenotypes based on the formation of α1 protease inhibitor allele product elastase complexes.
AUTHOR: Baumstark J.S.; Ting Lee C.; Luby R.J.
CORPORATE SOURCE: Dept. Obstet. Gynecol., Creighton Univ. Sch. Med., Omaha, Nebr. 68108, United States
SOURCE: Biochimica et Biophysica Acta, (1976) Vol. 446, No. 1, pp. 287-300.
CODEN: BBACAQ
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English

AB Up until now it has been assumed that the protease binding property of α1 protease inhibitor (α1PI) was destroyed by acid starch gel electrophoresis (pH 4.9). Analyses on acid starch gel blocks for pH and conductivity changes during and following a typical electrophoretic run showed that it was unlikely that the separating α1PI would be exposed to pH values lower than 6.2, and that the allele products, following the passage of the buffer front, were in an environment of constant pH (6.3), extremely low conductivity and high field strength. These results strongly suggested the likelihood that α1 PI would be chemically and physically unchanged as a result of exposure to acid starch gel electrophoresis. In order to test this likelihood, human serum was electrophoretically separated in acid starch gel and following electrophoresis, was immersed in 0.1 M diethylbarbiturate buffer, pH 8.6, containing 20 μg/ml of pancreatic elastase. The pH adjusted (8.15) and elastase impregnated starch gel layer was superimposed on hemoglobin agar for 2.5 h at 37°C followed by immersion of the hemoglobin agar layer in 1% NaCl overnight, distilled water for 2 h, drying under filter paper and staining. The results showed zones of undigested hemoglobin indicating, unequivocally, that the separated α1 PI allele products are capable of forming complexes with proteases and that α1 PI is not inactivated following exposure to acid starch gel electrophoresis. Densitometric analysis of the transparent stained zones on a clear agar gel background offers an alternative to analysis of the acid starch gel separated zones by antigen antibody crossed electrophoresis and as such is suitable for identification of α1 protease inhibitor phenotypes. Further, the method is specific for α1PI and a densitometric scan provides direct information relative to the protease binding capacity of the sample as well as the contribution of each α1PI allele product to that capacity.

L43 ANSWER 108 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights

reserved on STN
ACCESSION NUMBER: 77097254 EMBASE Full-text
DOCUMENT NUMBER: 1977097254
TITLE: Human alveolar macrophage (HAM) proteolytic enzyme levels in chronic obstructive pulmonary disease (COPD).
AUTHOR: Coudon W.L.; Harris J.O.
CORPORATE SOURCE: VA Hosp., Gainesville, Fla., United States
SOURCE: American Review of Respiratory Disease, (1976) Vol. 113, No. 4 II, pp. 216.
CODEN: ARDSBL
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
AB The occurrence of emphysema in patients with a deficiency of serum protease inhibitor and the production of emphysema in laboratory animals with elastolytic enzymes suggest that proteolysis may have a pathogenic role in COPD. HAMs of cigarette smokers are potential sources of enzymes because they are increased in number and have increased levels of elastase like esterase (HAM E) and acid protease (HAM P) when compared to HAMs of nonsmokers. To investigate the activity of HAM E and HAM P in COPD, macrophages were obtained by saline lavage of 16 freshly resected lungs of cigarette smokers undergoing surgery for suspected bronchogenic carcinoma. After red blood cell lysis by hypotonic shock, the HAMs were washed with balanced salt solution and collected by centrifugation at 250 g (4°C) for 10 minutes. Lavage samples containing > 10% leukocytes were not used for study. Cell viability determined by dye exclusion was 88%±1 (mean±SEM). HAM E assayed with t butyloxycarbonyl L alanine p nitrophenol as substrate was 5.2±.5 Δ A (347.5)/min/108 cells at pH 6.5, which is not different from normal cigarette smokers. HAM P (pH 3.5) was assayed using denatured hemoglobin as substrate and was 19.6±1.4 units/108 cells which is less than levels seen in normal smokers. This was probably due to lower viability of cells obtained from resected lungs. When HAM E and HAM P levels were compared to preoperative values for FVC, FEV1, DL(CO), and RV/TLC there were no significant correlations. This study suggests that COPD in cigarette smokers is not associated with greater HAM proteolytic enzyme levels than those of normal cigarette smokers. If proteolysis by HAM enzymes plays a role in the pathogenesis of COPD, it would more likely be related to chronic exposure of the lung to proteolytic enzymes, abnormal inhibitor/enzyme ratios, or possibly excessive release of enzymes.

L43 ANSWER 109 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 77097327 EMBASE Full-text
DOCUMENT NUMBER: 1977097327
TITLE: Pi Z subjects: a high risk group for chronic obstructive pulmonary disease.
AUTHOR: Rawlings W.; Cohen B.; Menkes H.; et al.
CORPORATE SOURCE: Johns Hopkins Med. Inst., Baltimore, Md., United States
SOURCE: American Review of Respiratory Disease, (1976) Vol. 113, No. 4 II, pp. 151.
CODEN: ARDSBL
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
AB Homozygous subjects for Pi Z phenotype (Pi Z) may present with chronic obstructive pulmonary disease at an early stage. However, the natural history of pulmonary function changes preceding overt disease is unknown. The authors studied pulmonary function in 20 Pi Z subjects ranging in age from 19 to 73. Forced expiratory volume in 1 second as a percentage of forced vital capacity (FEV1%), slope of phase III from the single breath nitrogen test (dN2) and single breath diffusing capacity for carbon monoxide (DL) were measured and the results regressed on age. The slopes of the regressions were compared with those of 310 nonsmokers (NS) and 305 smokers (S). For FEV1%, the slope for NS (mNS) was -0.203 (SE 0.021) %/year, the slope for S (m(S)) was -0.315 (SE 0.049), and the slope for Pi Z (m(Pi)(Z)) was -0.919 (SE 0.340). For dN2, mNS=0.005 (SE 0.003) %/liter/year, mS = 0.057 (SE 0.010), and mPi Z = 0.203 (SE 0.115). For DL, mNS=+0.328 (SE 0.082) % predicted/year, m(S)= -0.046 (SE 0.129), and mPi Z = -1.337 (SE 0.645). The decrease in pulmonary function with age may be the result of cumulative effects of repeated injury to the lungs. Degeneration of pulmonary function may be increased in the smoker because of increased exposure and Pi Z because of increased susceptibility. This raises the possibility that the best method for detecting the individual at risk (whether from increased exposure or increased susceptibility) is to measure changes in pulmonary function over a period of time prior to the development of overt disease.

L43 ANSWER 110 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 78001233 EMBASE Full-text
DOCUMENT NUMBER: 1978001233
TITLE: Value of alpha1 antitrypsin deficiency in heterozygotes with chronic obstructive bronchitis (Serbocroatian).
AUTHOR: Puganigg K.
CORPORATE SOURCE: Lungenabt., Landeskrankenh., Klagenfurt, Austria
SOURCE: Plucne Bolesti i Tuberkuloza, (1976) Vol. 28, No. 1-2, pp. 31-35.
CODEN: PLBTBZ
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
006 Internal Medicine
LANGUAGE: Serbo-Croatian

AB Alpha1 antitrypsin deficiency is the best known humoral proteinase inhibitor. It is correlated with diseases such as chronic obstructive emphysema, bronchiectases, hyaline membrane syndrome, cirrhosis of the liver in children, etc. The mean values in serum are different according to the data from the literature and a value of 220 ± 35 mg% is considered as a mean value. In the paper only patients with values below 170 mg% were taken into consideration of 468 patients with the diagnosis of chronic spastic bronchitis with emphysema, a heterozygote alpha1 antitrypsin deficiency was found in 21 patients. This finding is probably due to the effect of selection of patients in the pulmonary department. Alpha1 antitrypsin deficiency was not found to the only causal factor for the development of chronic spastic bronchitis, as environmental pollution and dust must also be present to provoke pulmonary disease.

L43 ANSWER 111 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 76074084 EMBASE Full-text
DOCUMENT NUMBER: 1976074084
TITLE: Protease inhibitors in chronic obstructive pulmonary disease.
AUTHOR: Barnett T.B.; Gottovi D.; Johnson A.M.
CORPORATE SOURCE: Dept. Med., Univ. North Carolina Sch. Med., Chapel Hill, N.C. 27514, United States
SOURCE: AMER.REV.RESP.DIS., (1975) Vol. 111, No. 5, pp. 587-593.
CODEN: ARRDAB
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
020 Gerontology and Geriatrics
006 Internal Medicine
LANGUAGE: English

AB Quantification of the major plasma protease inhibitors and genetic typing of α1 antitrypsin were done in 107 patients with chronic obstructive pulmonary disease and in 91 control subjects with normal ventilatory function who were similar with respect to age, race, and sex. There was a significant increase in frequency of the Pi(Z) gene and the Pi MZ phenotype of α1 antitrypsin among the patients when compared with the control subjects. No evidence for a primary deficiency of any other antiprotease was found; however, the mean concentration of inter α trypsin inhibitor was significantly lower in the patients than the control subjects, and moderate deficiency of α1 antichymotrypsin was noted in a few patients. These data indicate an increased risk of developing chronic obstructive pulmonary disease in persons with the Pi MZ phenotype of α1 antitrypsin and suggest a possible relationship between these diseases and low serum concentrations of inter α trypsin inhibitor.

L43 ANSWER 112 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 76080450 EMBASE Full-text
DOCUMENT NUMBER: 1976080450
TITLE: [Mucosal specific protease inhibitors in the bronchial mucus in cases of severe chronic obstructive bronchitis and α1 antitrypsin deficiency].
SCHLEIMHAUTSPEZIFISCHE PROTEASEINHIBITOREN IM BRONCHIALSCHLEIM BEI SCHWERER CHRONISCH OBSTRUKTIVER BRONCHITIS UND BEI α1 ANTITRYPSINMANGELSYNDROM.

AUTHOR: Rasche B.; Hochstrasser K.; Marcic I.; Ulmer W.T.
CORPORATE SOURCE: Med. Abt., Silik. Forsch. Inst. Bergbau Berufsgenossenschaft, Bochum, Germany
SOURCE: Respiration, (1975) Vol. 32, No. 5, pp. 340-354. CODEN: RESPBD
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
LANGUAGE: German

AB In the bronchial mucus of 40 patients with chronic obstructive airway diseases, proteolytic activities, the total protein concentrations, α1 antitrypsin, α1 antichymotrypsin, and the free and bound proteinase inhibitors were measured together with the total proteinase inhibition against trypsin and chymotrypsin. Without exception, free proteinase inhibitors were found together with proteolytic activities. The free to bound inhibitor rate was approximately 1:1. α1 antitrypsin and α1 antichymotrypsin were measured in sputum only in very low concentrations. One patient with α1 antitrypsin deficiency had no α1 antitrypsin, but high concentrations of total proteinase inhibitor (free and bound being in the same relation) in his bronchial mucus. In the alveolar part of the lung, the humoral proteinase inhibitors were effective. In the bronchial part of the lung, the specific mucosal inhibitors had decided importance. The proteinase inhibition of the mucosa specific inhibitors is probably of great importance for the pathogenesis of airway obstruction, while the humoral proteinase inhibitors are responsible for the pathogenesis of emphysema.

L43 ANSWER 113 OF 128 EMBASE
ACCESSION NUMBER: 76007708 EMBASE Full-text
DOCUMENT NUMBER: 1976007708
TITLE: Serum trypsin inhibitory capacity and Pi phenotypes. I. Methods and control values.
AUTHOR: Rynbrandt D.J.; Ihrig J.; Kleinerman J.
CORPORATE SOURCE: Div. Pathol. Res., St Luke's Hosp., Cleveland, Ohio 44104, United States
SOURCE: American Journal of Clinical Pathology, (1975) Vol. 63, No. 2, pp. 251-260. CODEN: AJCPAI
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English

AB Serum trypsin inhibitory capacity determinations are of considerable value in detecting genetically determined types of obstructive pulmonary disease and hepatic disease. These determinations must frequently be followed by determination of protease inhibitor (Pi) phenotype in order to confirm the diagnosis. Pi phenotyping has been a specialized and time consuming procedure, and suggested improvements in the methodology and techniques may make it more generally applicable as a clinical laboratory procedure. The prevalence of phenotypes other than MM in a group of 700 control sera from blood donors is reported as a baseline to evaluate typically American populations of mixed ethnic and racial characteristics. There are suggestive differences in prevalences of S and Z genes relating to ethnic stock and racial groups. It is important when comparing the prevalences of S and Z genes in diseased populations to use control groups of similar ethnic and racial compositions. Pi phenotyping is a necessary laboratory procedure in the diagnosis of certain forms of genetically determined chronic obstructive pulmonary disease and hepatic disease. The distributions of all serum protease inhibitory capacity values and those for S and Z Pi phenotypes are shown.

L43 ANSWER 114 OF 128 EMBASE
ACCESSION NUMBER: 75189945 EMBASE Full-text
DOCUMENT NUMBER: 1975189945
TITLE: [Effect of the protease inhibitor aprotinin on pulmonary function and on inhibitory activity of sputum in patients with chronic obstructive bronchitis]. UBER DIE WIRKUNG DES PROTEASEINHIBITORS APROTININ AUF DIE LUNGENFUNKTION SOWIE DIE INHIBITORISCHE AKTIVITAT DES SPUTUMS BEI PATIENTEN MIT CHRONISCH OBSTRUKTIVER BRONCHITIS.
AUTHOR: Rasche B.; Marcic I.; Ulmer W.T.

CORPORATE SOURCE: Med. Abt., Silikose Forsch. Inst., Bergbau Berufsgenossensch., Bochum, Germany
SOURCE: Arzneimittel-Forschung/Drug Research, (1975) Vol. 25, No. 1, pp. 110-116.
CODEN: ARZNAD
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
LANGUAGE: German

AB The authors investigated whether a substitution of protease inhibitor deficiency is indicated in cases of chronic obstructive airway disease. As a therapeutic possibility, aprotinin isolated from bovine organs (Trasylol), which in vitro inhibits sputum proteases up to 80% was tested. Besides infusion, inhalation was chosen for application by which a protease inhibition could be attained. An inhibition of the course of illness was observed, associated with a good tolerance of the preparation. Whether a therapy applying the addition of protease inhibitor is reasonable in the long run in chronic diseases cannot yet be concluded from these investigations.

L43 ANSWER 115 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 76158147 EMBASE Full-text
DOCUMENT NUMBER: 1976158147
TITLE: [Alpha 1 antitrypsin and the pathogenesis of chronic obstructive respiratory disease].
PATHOGENETISCHE BEDEUTUNG DES ALPHA 1 ANTITRYPSINS BEI CHRONISCH OBSTRUKTIVEN ATEMWEGSERKRANKUNGEN.
AUTHOR: Geisler L.S.; Rost H.D.; Bachmann G.W.; Vogel F.
CORPORATE SOURCE: Med. Univ. Klin., Bonn, Germany
SOURCE: PNEUMONOLOGIE, (1975) Vol. 152, No. 1-3, pp. 93-104.
CODEN: PNMGAU
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
006 Internal Medicine
LANGUAGE: German

AB α1 Antitrypsin deficiency only plays a subordinate role in the pathogenesis of chronic obstructive pulmonary disease. The majority of 120 patients studied had an elevated α1 antitrypsin serum concentration, which supports the hypothesis that protease induced alterations in the sensitivity of the cholinergic receptors in the bronchial tree contribute to the airway obstruction. Studies in two families with α1 antitrypsin deficiency demonstrated that non obstructive emphysema of the lung is also encountered in this disorder. Pulmonary abnormalities were not seen in 3 out of 5 homozygotes. The results indicate that in addition to the interaction between proteases and protease inhibitors, other factors must be considered in the etiology of the airway obstruction.

L43 ANSWER 116 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 76158140 EMBASE Full-text
DOCUMENT NUMBER: 1976158140
TITLE: Characterization of masked specific proteinase inhibitor from bronchial secretions in purulent sputum as complex with leucocytic proteinases.
AUTHOR: Hochstrasser K.; Schorn K.; Rasche B.; et al.
CORPORATE SOURCE: Biochem. Lab., HNO Klin., Univ. Munchen, Germany
SOURCE: PNEUMONOLOGIE, (1975) Vol. 152, No. 1-3, pp. 15-24.
CODEN: PNMGAU
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
006 Internal Medicine
LANGUAGE: English

AB By gel filtration and ion exchange chromatography, proteinase bound proteinase inhibitor, specific for mucous membranes was isolated from purulent sputum of patients with obstructive airway diseases. The isolated material contains 25% complexed inhibitor. The complex interacts with specific anti inhibitor serum and anti inter alpha trypsin inhibitor serum. With anti leucocytic proteinase serum an interaction is observed, too. The proteinase part of the complexed inhibitor therefore is a leucocytic proteinase.

L43 ANSWER 117 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 75191749 EMBASE Full-text
DOCUMENT NUMBER: 1975191749
TITLE: [Clinical and statistical notes on alpha 1 anti trypsin levels in 130 cases of chronic bronchopneumopathy].
L'ALFA 1 ANTITRIPSINA IN PATOLOGIA UMANA. RILIEVI CLINICO STATISTICI SULL'α 1 AT NELLE BRONCOPNEUMOPATIE CRONICHE. CONTRIBUTO PERSONALE.
AUTHOR: Dalmasso F.; Cardellino G.; Garbagni R.
CORPORATE SOURCE: Ist. Clin. Med. Gen. Ter. Med., Univ. Studi, Torino, Italy
SOURCE: Minerva Medica, (1974) Vol. 65, No. 89, pp. 4671-4689.
CODEN: MIMEAO
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
006 Internal Medicine
LANGUAGE: Italian

AB The globulin alpha 1 antitrypsin (α1 AT) forms 80% of the serum proteolytic inhibitor complex. Blood levels are genetically linked to codominant alleles that determine the phenotype of the so called protease inhibitor system. In chronic obstructive bronchopneumopathy, α1 AT may be totally or partly absent. Total deficiency (homozygote) is almost always associated with essential pulmonary emphysema. Incomplete deficiency may be observed in healthy subjects, but predisposes patients to various forms of bronchopneumopathy, and is often associated with them. 130 cases of asthma, emphysema, chronic bronchitis, lung cancer and pneumopathy associated with other diseases were examined. Total deficiency was not observed, while partial deficiency in 16 cases (12.3%) was highest in asthmatics (22.2%), followed by subjects with various forms (11.8%), chronic bronchitis (11.1%), emphysema (7.5%), and cancer (0%). α1 AT levels were lowest in the asthmatics. Changes following cortisone management show no constant pattern: increase in values in 4 cases, reduction in 3, no change in 4. The same impression is gained from the literature. Study of α1 AT suggests a new hypothesis for the pathogenesis of pulmonary emphysema, whereby proteolytic enzymes, particulary those derived from leukocytes, alveolar macrophages and bacteria may be supposed to lyse the alveolar wall and lung elastic fibres. Emphysema may result when such lysis is the result of abundant enzyme production, due either to infection, tobacco smoke and atmospheric and industrial pollution, or depressed antiprotease activity on the part of α1 AT.

L43 ANSWER 118 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 75102751 EMBASE Full-text
DOCUMENT NUMBER: 1975102751
TITLE: Deficiency of α1 antitrypsin (Dutch).
AUTHOR: Jansveld A.F.; Dijkman J.H.
CORPORATE SOURCE: Afd. Longz., Univ. Klin. Inw. Ziekten, St Radboud Ziekenh., Nijmegen, Netherlands
SOURCE: Nederlands Tijdschrift voor Geneeskunde, (1974) Vol. 118, No. 36, pp. 1366-1372.
CODEN: NETJAN
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
015 Chest Diseases, Thoracic Surgery and Tuberculosis
023 Nuclear Medicine
014 Radiology
LANGUAGE: Dutch

AB Prompted by finding 3 patients with a deficiency of α1 antitrypsin, the authors discuss the symptoms, genetics, pathophysiology and prevalence of this hereditary disease. Individuals who are homozygotic for the Pi(Z) gene (phenotype PiZZ) have a serum level of α1 antitrypsin amounting to only 15% of the normal value. In most cases this leads to pulmonary emphysema, often in the young adult, with the symptoms of chronic obstructive pulmonary disease, type A. Deficiency of α1 antitrypsin also causes a predisposition to neonatal hepatitis and cirrhosis of the liver in children and adults. The pulmonary lesions are probably due to gradual disintegration of lung tissue resulting from insufficient inhibition of the proteases released from macrophages and leukocytes. The prevalence of phenotype PiZZ is estimated to be 1:1000 to 1:2000 births. Intermediary α1 antitrypsin deficiency (phenotype PiMZ) occurs in 5 to 6% of the population, but the symptoms in these cases are usually mild.

L43 ANSWER 119 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 75174184 EMBASE Full-text
DOCUMENT NUMBER: 1975174184
TITLE: Alpha 1 antitrypsin deficiency and pulmonary disease.
AUTHOR: Sun T.; Kurtz S.; Copeland B.E.
CORPORATE SOURCE: Dept. Pathol., New England Deacon Hosp., Boston, Mass. 02215, United States
SOURCE: American Journal of Clinical Pathology, (1974) Vol. 62, No. 6, pp. 725-731.
CODEN: AJCPAI
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
005 General Pathology and Pathological Anatomy
022 Human Genetics
015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
007 Pediatrics and Pediatric Surgery
LANGUAGE: English

AB The early development of chronic obstructive pulmonary disease in individuals with alpha 1 antitrypsin deficiency may be potentially preventable. A general screening for alpha 1 antitrypsin in patients with chronic obstructive pulmonary disease and their family members seems advisable because these families have a high incidence of alpha 1 antitrypsin deficiency. After a comparison study of electrophoresis, trypsin inhibitory capacity, phenotyping, and radial immunodiffusion technics, the authors recommend radial immunodiffusion as a screening test for alpha 1 antitrypsin deficiency. It is simple, correlates well with trypsin inhibitory capacity and phenotyping, and provides quantitative information for preliminary classification. A parallel determination of stimulated and nonstimulated alpha 1 antitrypsin levels is suggested.

L43 ANSWER 120 OF 128 MEDLINE on STN DUPLICATE 22

ACCESSION NUMBER: 74091956 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 4811786
TITLE: Prevalence of abnormal protease inhibitor phenotypes in patients with chronic obstructive lung disease.
AUTHOR: Mittman C; Lieberman J; Rumsfeld J
SOURCE: American review of respiratory disease, (1974 Feb) 109 (2) 295-6.
Journal code: 0370523. ISSN: 0003-0805.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197404
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19740402

L43 ANSWER 121 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 75091413 EMBASE Full-text
DOCUMENT NUMBER: 1975091413
TITLE: [Free and combined protease inhibitors in bronchial mucus in patients with extended chronic obstructive airway diseases].
FREIE UND GEBUNDENE PROTEASENINHIBITOREN IM BRONCHIALSCHLEIM VON PATIENTEN MIT LANGJAHRIGEN CHRONISCH OBSTRUKTIVEN LUNGENERKRANKUNGEN.
AUTHOR: Hochstrasser K.; Rasche B.; Reichert R.; Hochgesand K.
CORPORATE SOURCE: HNO Klin., Univ. Munchen, Germany
SOURCE: PNEUMONOLOGIE, (1974) Vol. 150, No. 2-4, pp. 253-259.
CODEN: PNMGAU
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
020 Gerontology and Geriatrics
005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis

LANGUAGE: German

AB The inhibitory effect of proteases in the bronchial space is due to a mucus specific low molecular inhibitor in 80% of cases. In native secretion larger amounts of inhibitors are present in a masked form, i.e. a complex is formed with proteases, in case of banal infections usually leukocyte protease. In the sputa of patients with moderately severe to severe airway obstruction of some years' standing, antiproteolytic and proteolytic activity is found simultaneously. In the case of antiproteolytic activity, the mucus specific protease inhibitor is also predominant over humoral inhibitors in the sputum. In persons who have been ill for some years, it seems that proteolytic enzymes that may be of bacterial origin or tissue proteases that cannot be inhibited by the natural mucosa inhibitor are dominant in the sputa. Present investigations suggest that elevated proteolysis favors the development of obstructions.

L43 ANSWER 122 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 75093532 EMBASE Full-text
DOCUMENT NUMBER: 1975093532
TITLE: Antitrypsin and its deficiency.
AUTHOR: Kueppers F.; Black L.F.
CORPORATE SOURCE: Mayo Clin. Found., Rochester, Minn., United States
SOURCE: AMER.REV.RESP.DIS., (1974) Vol. 110, No. 2, pp. 176-194.
CODEN: ARRDAB
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
006 Internal Medicine
025 Hematology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English

AB α1 Antitrypsin is a glycoprotein in human serum that inhibits several proteases. Its normal concentration is 180 to 280 mg/100 ml. Under various conditions, including pregnancy and inflammation, its level in serum increases considerably. α1 Antitrypsin is a polymorphic protein. More than 20 phenotypes can be distinguished by electrophoretic techniques. The available family data are consistent with the hypothesis of a single autosomal locus (Pi) with multiple co dominant alleles. Of particular interest are alleles that lead to lower than normal concentrations of α1 antitrypsin in serum, namely, PiZ, PiS and Pi-. PiZ homozygotes have α1 antitrypsin concentrations of approximately 20 mg/100 ml. These persons carry a high risk of developing chronic obstructive pulmonary disease, which generally has its onset during the fourth decade of life. With advancing age, the proportion of all ZZ homozygotes who have obstructive pulmonary disease eventually may be as high as 80%. Heterozygotes with phenotypes MZ, MS, and intermediate α1 antitrypsin levels also may be predisposed to obstructive pulmonary disease, but to a lesser degree. Cigarette smoking apparently accelerates the deterioration of pulmonary functions in homozygotes and heterozygotes for a deficiency gene (mostly PiZ). Uninhibited proteases of leukocytic origin probably are partly responsible for the damage to the lung in the absence of the major protease inhibitor. Neonatal hepatitis and cirrhosis of the liver also are found in association with homozygosity for PiZ. The risk of an infant with α1 antitrypsin deficiency developing neonatal hepatitis may be between 20 and 30%.

L43 ANSWER 123 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 74167968 EMBASE Full-text
DOCUMENT NUMBER: 1974167968
TITLE: [Proteolysis and obstructive lung emphysema].
PROTEOLYSE UND OBSTRUKTIVES LUNGENEMPHYSEM.
AUTHOR: Reichert R.; Hochstrasser K.; Hochgesand K.
CORPORATE SOURCE: Biochem. Lab., HNO Klin., Univ. Munchen, Germany
SOURCE: Munchener Medizinische Wochenschrift, (1974) Vol. 116, No. 4, pp. 173-176.
CODEN: MMWOAU
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
006 Internal Medicine
LANGUAGE: German

AB There is a great statistical significance for the development of obstructive emphysema of the lung in hereditary deficiency of alpha 1 antitrypsin in the blood serum. Since alpha 1 antitrypsin is a protease inhibitor according to its biochemical action, particular

importance is attributed to proteolytic processes. The proteases participating in this originate from disintegrating leukocytes. Complexes between alpha 1 antitrypsin or mucous membrane inhibitors and proteases can be demonstrated in the sputum. The quantity of these complexes is a measure for the demands on the inhibiting system by the proteases produced. If the system is overstrained, proteolytic activity is released in the secretions, the effect of which leads to the development of respiratory tract obstructions.

L43 ANSWER 124 OF 128 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1974:70189 BIOSIS Full-text
DOCUMENT NUMBER: PREV197410070189; BR10:70189
TITLE: ALPHA-1 ANTI TRYPSIN PROTEASE INHIBITOR TYPES PREVALENCE STUDIES.
AUTHOR(S): SCHWARTZ R H; HALL W; HYDE R; VAN ESS J D
SOURCE: Journal of Allergy and Clinical Immunology, (1974) Vol. 53, No. 2, pp. 108-109.
CODEN: JACIBY. ISSN: 0091-6749.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: Unavailable

L43 ANSWER 125 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 74163969 EMBASE Full-text
DOCUMENT NUMBER: 1974163969
TITLE: Screening for α1 antitrypsin deficiency.
AUTHOR: Mittman C.; Lieberman J.
CORPORATE SOURCE: Respirat. Dis. Dept., City Hope Nat. Med. Cent., Duarte, Calif., United States
SOURCE: Israel Journal of Medical Sciences, (1973) Vol. 9, No. 9-10, pp. 1311-1318.
CODEN: IJMDAI
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
025 Hematology
006 Internal Medicine
LANGUAGE: English
AB Recent studies of the relationship between α1 antitrypsin deficiency (AATD) and both chronic obstructive lung disease and liver disease suggest that screening for this inherited plasma protein deficiency may be desirable. It has been reported that a significant fraction of cases of chronic obstructive lung disease are associated with the protease inhibitor deficiency in its severe and intermediate form. Liver diseases, particularly neonatal hepatitis and possibly other abnormalities in children and adults, are associated with the severe and possibly with the milder deficiency states. However, not all carriers of the deficiency develop overt lung or liver disease. This paper reviews the current understanding of the relationship between disease and AATD and considers the justification for screening programs for this protein defect.

L43 ANSWER 126 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 74190474 EMBASE Full-text
DOCUMENT NUMBER: 1974190474
TITLE: Human alpha1 antitrypsin.
AUTHOR: Kueppers F.
CORPORATE SOURCE: Inst. Hum. Genet., Univ. Hamburg, Germany
SOURCE: Environmental Research, (1973) Vol. 6, No. 4, pp. 403-423.
CODEN: ENVRAL
DOCUMENT TYPE: Journal
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
029 Clinical Biochemistry
002 Physiology
025 Hematology
LANGUAGE: English
AB Homozygotes for an alpha1 antitrypsin (at) deficiency gene (ZZ) carry a considerable risk of chronic obstructive lung disease and emphysema which manifest themselves between the ages of 30 and 60 yr but typically during the fourth decade of life. With advancing age the proportion of those with lung disease among all alpha1 at deficient individuals

becomes greater and may eventually be as high as 80% or higher depending somewhat on environmental and other factors. Heterozygotes (MZ) are probably also at risk but to a much lesser degree than homozygotes; they are only approximately twice as likely to develop chronic obstructive lung disease than homozygous normals (MM). Liver disease has also been recognized in association with alpha1 (at) deficiency. It may occur as neonatal hepatitis with subsequent cirrhosis or just as cirrhosis during adulthood. The proportion of patients with liver disease among all homozygotes for the deficiency ranges perhaps between 10 and 30%. Although alpha1 at may have an important function in respiratory distress syndrome and hyaline membrane disease there is at present no clear evidence linking these conditions or their clinical course to alpha1 at deficiency. The results on sex chromosome mosaicism as related to alpha1 at heterozygosity of the mother are contradictory.

L43 ANSWER 127 OF 128 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 23

ACCESSION NUMBER: 1974:146503 BIOSIS Full-text
DOCUMENT NUMBER: PREV197457046203; BA57:46203
TITLE: ANTI TRYPSIN DEFICIENCY AND ABNORMAL PROTEASE INHIBITOR PHENOTYPES.
AUTHOR(S): MITTMAN C; BARBELA T; LIEBERMAN J
SOURCE: Archives of Environmental Health, (1973) Vol. 27, No. 3, pp. 201-206.
CODEN: AEHLAU. ISSN: 0003-9896.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable

L43 ANSWER 128 OF 128 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 74005886 EMBASE Full-text
DOCUMENT NUMBER: 1974005886
TITLE: [Possibilities for the assessment of chronic obstructive airway disease by analysis of the sputum]. MOGLICHKEITEN ZUR BEURTEILUNG CHRONISCH OBSTRUKTIVER ATEMWEGSERKRANKUNGEN MIT HILFE VON ANALYSEN IM BRONCHIALSCHLEIM.
AUTHOR: Rasche B.; Baving G.; Ulmer W.T.
CORPORATE SOURCE: Med. Abt., Silikose Forsch. Inst., Bergbau Berufsgenossensch., Bochum, Germany
SOURCE: PNEUMONOLOGIE, (1973) Vol. 148, No. 2, pp. 141-159.
CODEN: PNMGAU
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: German

AB The sputum of patients affected with chronic obstructive airway diseases contains among other things, immunoglobulins, mainly IgA, as well as proteolytic ferments and their inhibitors. Parameters were analyzed daily in 8 patients and values compared with the clinical course of the disease to determine if values measured allowed any clinical conclusions to be drawn. Investigations showed a rise in the IgA level in the sputum during the administration of glucocorticoids and antibiotics, with large daily variations. Proteolytic ferment activity showed only minor alterations during this treatment. Alpha1 antitrypsin, the most important protease inhibitor in the organism, is of less importance for the lungs and is more important as a sign of inflammation. Ferment inhibitors intrinsic to the sputum seem to be available in varying concentrations in the bronchial space during inactivation of the proteases. The values measured at the daily examinations varied considerably in all patients.

=> log y

```
FILE 'HOME' ENTERED AT 11:35:07 ON 15 NOV 2005

=> file .Nash
=> s cystic fibrosis and inhibitor and protease
L1          142 FILE MEDLINE
L2          124 FILE CAPLUS
L3          236 FILE SCISEARCH
L4           12 FILE LIFESCI
L5          119 FILE BIOSIS
L6          109 FILE EMBASE

TOTAL FOR ALL FILES
L7          742 CYSTIC FIBROSIS AND INHIBITOR AND PROTEASE

=> s cystic fibrosis and inhibitor and (protease or proteinase)
L8          224 FILE MEDLINE
L9          214 FILE CAPLUS
L10         329 FILE SCISEARCH
L11          21 FILE LIFESCI
L12         185 FILE BIOSIS
L13         282 FILE EMBASE

TOTAL FOR ALL FILES
L14        1255 CYSTIC FIBROSIS AND INHIBITOR AND (PROTEASE OR PROTEINASE)

=> s l14 and kunitz
L15           3 FILE MEDLINE
L16           6 FILE CAPLUS
L17           2 FILE SCISEARCH
L18           0 FILE LIFESCI
L19           4 FILE BIOSIS
L20           1 FILE EMBASE

TOTAL FOR ALL FILES
L21          16 L14 AND KUNITZ

=> dup rem l21
PROCESSING COMPLETED FOR L21
L22           11 DUP REM L21 (5 DUPLICATES REMOVED)

=> d ibib abs 1-11

L22  ANSWER 1 OF 11  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
ACCESSION NUMBER:    2004:151663  BIOSIS Full-text
DOCUMENT NUMBER:     PREV200400154674
TITLE:               Polynucleotide molecules encoding proteins having
                     proteinase inhibitor activity.
AUTHOR(S):           Davies, Christopher [Inventor, Reprint Author]; Chen,
                     Dadong [Inventor]; Roczniak, Steve [Inventor]
CORPORATE SOURCE:    Walnut Creek, CA, USA
                     ASSIGNEE: Bayer Pharmaceuticals Corporation
PATENT INFORMATION: US 6689582 20040210
SOURCE:              Official Gazette of the United States Patent and Trademark
                     Office Patents, (Feb 10 2004) Vol. 1279, No. 2.
                     http://www.uspto.gov/web/menu/patdata.html. e-file.
                     ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE:       Patent
LANGUAGE:            English
ENTRY DATE:          Entered STN: 17 Mar 2004
                     Last Updated on STN: 17 Mar 2004
AB     BTL.010 is a novel human serine proteinase inhibitor of the Kunitz family that exhibits
       greater potency towards neutral serine proteinases, particularly leukocyte elastase and
       proteinase 3 than towards trypsin-like proteinases. BTL.010, or variants thereof, may be
       employed as therapeutics in diseases such as emphysema, idiopathic pulmonary fibrosis,
       adult respiratory distress syndrome, cystic fibrosis, rheumatoid arthritis, organ failure,
       and glomerulonephritis in which uncontrolled proteolysis due to neutral serine proteinase
       activity results in tissue damage.


L22  ANSWER 2 OF 11  CAPLUS  COPYRIGHT 2005 ACS on STN
```

ACCESSION NUMBER: 2003:633891 CAPLUS Full-text
DOCUMENT NUMBER: 139:174845
TITLE: Recombinant production of albumin-fused Kunitz domain serine protease-inhibiting peptides with extended shelf-life, for treating cystic fibrosis, hereditary angioedema and cancer
INVENTOR(S): Hauser, Hans-peter; Weimer, Thomas; Romberg, Val; Kee, Scott M.; Sleep, Darrell; Ladner, Robert Charles; Ley, Arthur C.
PATENT ASSIGNEE(S): Aventis Behring GmbH, Germany; Aventis Behring GmbH; Delta Biotechnology Limited; Dyax Corporation; et al.
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003066824	A2	20030814	WO 2003-US3616		20030207
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2485064	AA	20030814	CA 2003-2485064		20030207
EP 1572930	A2	20050914	EP 2003-737682		20030207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2005222023	A1	20051006	US 2005-503834		20050413
PRIORITY APPLN. INFO.:			US 2002-355547P	P	20020207
			WO 2003-US3616	W	20030207

AB The invention relates to proteins comprising serine protease inhibiting peptides, such as Kunitz domain peptides fused to albumin, or fragments or variants thereof. These fusion proteins are herein collectively referred to as 'albumin fusion proteins of the invention.'. These fusion proteins exhibit extended shelf-life and/or extended or therapeutic activity in solution The invention encompasses, therapeutic albumin fusion proteins, compns., pharmaceutical compns., formulations and kits. The invention also encompasses nucleic acid mols. encoding the albumin fusion proteins of the invention, as well as vectors containing these nucleic acids, host cells transformed with these nucleic acids and vectors, and methods of making the albumin fusion proteins of the invention using these nucleic acids, vectors, and/or host cells. The invention also relates to compns. and methods for inhibiting neutrophil elastase, kallikrein, and plasmin. The invention further relates to compns. and methods for treating cystic fibrosis and cancer. The present invention also relates to bifunctional (or multifunctional) fusion proteins in which albumin is coupled to two (or more) Kunitz domain peptides, optionally different Kunitz domain peptides. Such bifunctional (or multifunctional) fusion proteins having different Kunitz domain peptides are expected to have an improved drug resistance profile as compared to an albumin fusion protein comprising only one type of Kunitz domain peptide.

L22 ANSWER 3 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:395600 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300395600
TITLE: Use of phage display to identify potent and specific protease inhibitors.
AUTHOR(S): Nixon, A. E. [Reprint Author]
CORPORATE SOURCE: Research and Technology, Dyax Corp., Cambridge, MA, 02139, USA
SOURCE: Biopolymers, (2003) Vol. 71, No. 3, pp. 398. print.
Meeting Info.: 18th American Peptide Symposium on Peptide Revolution: Genomics, Proteomics and Therapeutics. Boston, MA, USA. July 19-23, 2003. American Peptide Society.
ISSN: 0006-3525 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Aug 2003
Last Updated on STN: 27 Aug 2003

L22 ANSWER 4 OF 11 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002172859 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11867337
TITLE: Protection against acute lung injury by intravenous or intratracheal pretreatment with EPI-HNE-4, a new potent neutrophil elastase inhibitor.
COMMENT: Comment in: Am J Respir Cell Mol Biol. 2002 Mar;26(3):266-8. PubMed ID: 11867332
AUTHOR: Delacourt Christophe; Herigault Sabine; Delclaux Christophe; Poncin Alain; Levame Micheline; Harf Alain; Saudubray Francois; Lafuma Chantal
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Scientifique, Faculte de Medecine, Creteil, France.
SOURCE: American journal of respiratory cell and molecular biology, (2002 Mar) 26 (3) 290-7.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020322
Last Updated on STN: 20020403
Entered Medline: 20020329

AB Excessive accumulation of active neutrophil elastase (NE) in pulmonary fluids and tissues of patients with cystic fibrosis (CF) is thought to act on the lungs, compromising their structure and function. The aim of this study was to investigate the in vitro and in vivo protective effect of a new, rapidly acting, potent (Ki = 5.45 x 10(-12) M and Kon = 8 x 10(6) M(-1) s(-1)) and specific human NE inhibitor, EPI-HNE-4, engineered from the Kunitz domain. The results demonstrated that this inhibitor was able to (i) effectively inhibit in vitro the high levels of active NE present in a medium as complex as sputum from children with CF, with a measured IC(50) equal or close to the calculated IC(50) in 60% of cases, and (ii) almost completely block (91%) the N-formyl-methionine-leucine-phenylalanine- induced migration of purified human neutrophils across a Matrigel basement membrane. Intratracheal administration (250, 175, or 100 microg per rat) of the inhibitor 5 min before instillation of pure human NE (HNE) (150 microg per rat) to rats induced effective, dose-dependent protection of the lungs, 4 h later, from hemorrhage, serum albumin leakage, residual active NE, and discrete neutrophil influx in air spaces induced by instillation of pure HNE. Intravenous administration (3 mg per rat) of EPI-HNE-4, 15 min before instillation of the soluble fraction of pooled sputum (delivering 120 microg of active NE per rat) from children with CF, effectively reduced (64%), 4 h later, the massive neutrophil influx induced by sputum instillation. Overall, these data strongly suggest that associated aerosol and systemic administration of EPI-HNE-4 would be beneficial in the treatment of CF.

L22 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2001:75295 CAPLUS Full-text
DOCUMENT NUMBER: 134:141769
TITLE: Protein having proteinase inhibitor activity
INVENTOR(S): Davies, Christopher; Chen, Dadong; Roczniak, Steve
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 17 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6180607	B1	20010130	US 1999-369494	19990805
US 6689582	B1	20040210	US 2000-569670	20000512
PRIORITY APPLN. INFO.:			US 1999-369494 A3	19990805

AB BTL.010 is a novel human serine proteinase inhibitor of the Kunitz family that exhibits greater potency towards neutral serine proteinases, particularly leukocyte elastase-, and proteinase 3, than towards trypsin-like proteinases . BTL.010, or variants thereof, may be employed as therapeutics in diseases such as emphysema, idiopathic pulmonary fibrosis, adult respiratory distress syndrome, cystic fibrosis, rheumatoid arthritis, organ failure, and glomerulonephritis in which uncontrolled proteolysis due to neutral serine proteinase activity results in tissue damage.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:703054 CAPLUS Full-text
DOCUMENT NUMBER: 135:267267
TITLE: Protein and cDNA sequences of a novel human protein BTL.009 having proteinase inhibitor activity
INVENTOR(S): Delaria, Kathy; Roczniak, Steve; Davies, Christopher
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: U.S., 16 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6294648	B1	20010925	US 1999-358569	19990720
PRIORITY APPLN. INFO.:			US 1999-358569	19990720

AB The invention provides protein and cDNA sequences of a novel human protein BTL.009, which is a novel human serine proteinase inhibitor of the Kunitz family that exhibits greater potency towards neutral serine proteinases, particularly leukocyte elastase, and chymotrypsin than towards trypsin-like proteinases. BTL.009 has been identified as a member of the Kunitz family of proteinase inhibitors based on the presences of the conserved six cysteines observed in all members of this family. BTL.009, or variants thereof, may be employed as therapeutics in diseases such as emphysema, idiopathic pulmonary fibrosis, adult respiratory distress syndrome, cystic fibrosis, rheumatoid arthritis, organ failure, and glomerulonephritis in which uncontrolled proteolysis due to neutral serine proteinase activity results in tissue damage.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 11 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001336099 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11404240
TITLE: Na+ transport in normal and CF human bronchial epithelial cells is inhibited by BAY 39-9437.
COMMENT: Comment in: Am J Physiol Lung Cell Mol Physiol. 2001 Jul;281(1):L13-5. PubMed ID: 11404239
AUTHOR: Bridges R J; Newton B B; Pilewski J M; Devor D C; Poll C T; Hall R L
CORPORATE SOURCE: Department of Cell Biology and Physiology, University of Pittsburgh, Pittsburgh, Pennsylvania 15261, USA..
bbridges+@pitt.edu
SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2001 Jul) 281 (1) L16-23.
Journal code: 100901229. ISSN: 1040-0605.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB To test the hypothesis that Na+ transport in human bronchial epithelial (HBE) cells is regulated by a protease-mediated mechanism, we investigated the effects of BAY 39-9437, a recombinant Kunitz -type serine protease inhibitor, on amiloride-sensitive short-circuit current of normal [non-cystic fibrosis (CF) cells] and CF HBE cells. Mucosal treatment of non-CF and CF HBE cells with BAY 39-9437 decreased the short-circuit current, with a half-life of approximately 45 min. At 90 min, BAY 39-9437 (470 nM) reduced Na+ transport by

approximately 70%. The inhibitory effect of BAY 39-9437 was concentration dependent, with a half-maximal inhibitory concentration of approximately 25 nM. Na+ transport was restored to control levels, with a half-life of approximately 15 min, on washout of BAY 39-9437. In addition, trypsin (1 microM) rapidly reversed the inhibitory effect of BAY 39-9437. These data indicate that Na+ transport in HBE cells is activated by a BAY 39-9437-inhibitable, endogenously expressed serine protease. BAY 39-9437 inhibition of this serine protease maybe of therapeutic potential for the treatment of Na+ hyperabsorption in CF.

L22 ANSWER 8 OF 11 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001351318 EMBASE Full-text
TITLE: Na(+) transport in normal and CF human bronchial epithelial cells is inhibited by BAY 39-9437.
AUTHOR: Bridges R.J.; Newton B.B.; Pilewski J.M.; Devor D.C.; Poll C.T.; Hall R.L.
CORPORATE SOURCE: R.J. Bridges, Dept. of Cell Biology, Univ. of Pittsburgh, S310 Biomedical Science Tower, 3500 Terrace St., Pittsburgh, PA 15261, United States. bbridges+@pitt.edu
SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (2001) Vol. 281, No. 1 25-1, pp. L16-L23.
Refs: 33
ISSN: 1040-0605 CODEN: APLPE7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20011018
Last Updated on STN: 20011018

AB To test the hypothesis that Na(+) transport in human bronchial epithelial (HBE) cells is regulated by a protease-mediated mechanism, we investigated the effects of BAY 39-9437, a recombinant Kunitz -type serine protease inhibitor, on amiloride-sensitive short-circuit current of normal [non-cystic fibrosis (CF) cells] and CF HBE cells. Mucosal treatment of non-CF and CF HBE cells with BAY 39-9437 decreased the short-circuit current, with a half-life of .apprx.45 min. At 90 min, BAY 39-9437 (470 nM) reduced Na(+) transport by .apprx.70%. The inhibitory effect of BAY 39-9437 was concentration dependent, with a half-maximal inhibitory concentration of .apprx.25 nM. Na(+) transport was restored to control levels, with a half-life of .apprx.15 min, on washout of BAY 39-9437. In addition, trypsin (1 μM) rapidly reversed the inhibitory effect of BAY 39-9437. These data indicate that Na(+) transport in HBE cells is activated by a BAY 39-9437-inhibitable, endogenously expressed serine protease. BAY 39-9437 inhibition of this serine protease maybe of therapeutic potential for the treatment of Na(+) hyperabsorption in CF.

L22 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:441647 CAPLUS Full-text
DOCUMENT NUMBER: 133:84295
TITLE: Kunitz-type serine proteinase inhibitors for accelerating the rate of mucociliary clearance
INVENTOR(S): Hall, Roderick; Poll, Christopher T.; Newton, Benjamin B.; Taylor, William J. A.
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037099	A2	20000629	WO 1999-GB4381	19991222
WO 2000037099	A3	20001026		

W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,

LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,
SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2356404	AA	20000629	CA 1999-2356404	19991222
EP 1140150	A2	20011010	EP 1999-963636	19991222
EP 1140150	B1	20031119		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

JP 2002532558	T2	20021002	JP 2000-589209	19991222
AU 758832	B2	20030403	AU 2000-19878	19991222
AT 254473	E	20031215	AT 1999-963636	19991222
EP 1374891	A1	20040102	EP 2003-18789	19991222

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, LT, LV, FI, MK, CY, AL

ES 2209542	T3	20040616	ES 1999-963636	19991222
PRIORITY APPLN. INFO.:			US 1998-218913	A 19981222
			US 1999-441966	A 19991117
			EP 1999-963636	A3 19991222
			WO 1999-GB4381	W 19991222

AB The instant invention provides for a composition and method for using Kunitz-type serine protease inhibitors, e.g., aprotinin or bikunin, for stimulating the rate of mucociliary clearance of mucus and sputum in lung airways of subjects afflicted with mucociliary dysfunctions such as cystic fibrosis.

L22 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:466606 CAPLUS Full-text
DOCUMENT NUMBER: 119:66606
TITLE: Manufacture of Kunitz proteinase inhibitor domain of amyloid precursor protein (APP) for therapeutic use and for modelling of APP processing and amyloidosis
INVENTOR(S): Wagner, Steven L.; Siegel, Robert; Thill, Gregory P.; Harpold, Michael M.; Comer, William T.
PATENT ASSIGNEE(S): Salk Institute Biotechnology/Industrial Associates, Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9309233	A2	19930513	WO 1992-US9400	19921030
WO 9309233	A3	19930805		

W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KR, LK, MG, MN, MW, NO, PL,
RO, RU, SD, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF,
BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG

AU 9230610	A1	19930607	AU 1992-30610	19921030
PRIORITY APPLN. INFO.:			US 1991-785638	A2 19911031
			WO 1992-US9400	A 19921030

AB The Kunitz proteinase inhibitor (KPI) domain of the amyloid precursor protein is manufactured in yeast cells for use in the treatment of diseases such as Alzheimer's disease, coagulation disorders, and emphysema. An in vitro model of APP processing and disease origination involving addition of the KPI to cultured neuronal cells is described. A synthetic gene encoding residues 285-345 of APP fused to the yeast α-mating factor signal sequence was expressed from the AOX1 promoter in Pichia pastoris. The KPI produced was purified and partially sequenced, its amino acid composition determined, and its protease inhibitory activity examined The in vitro model was demonstrated.

L22 ANSWER 11 OF 11 MEDLINE on STN
ACCESSION NUMBER: 82093827 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6172220
TITLE: Protease binding by alpha 2 macroglobulin in

cystic fibrosis.
AUTHOR: Bridges M A; Applegarth D A; Johannson J; Wong L T; Davidson A G
SOURCE: Clinica chimica acta; international journal of clinical chemistry, (1982 Jan 5) 118 (1) 33-43. Journal code: 1302422. ISSN: 0009-8981.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198203
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19970203
Entered Medline: 19820322

AB The interaction of alpha 2 macroglobulin (alpha 2M) with exogenous proteases has been reported by others to be abnormal in cystic fibrosis (CF). We have re-examined these claims. Four parameters were considered:(1) the molar protease binding of alpha 2M; (2) the interaction of bovine cationic trypsin (BCT), complexed to alpha 2M, with low molecular mass substrate, benzoyl arginine ethyl ester (BAEE); (3) the stability of formed alpha 2 M-BCT complexes; and (4) the subunit structure of alpha 2M. We have found CF alpha 2M to be similar to control alpha 2M in every respect studied.

=> d his

(FILE 'HOME' ENTERED AT 11:35:07 ON 15 NOV 2005)

FILE 'MEDLINE, CAPLUS, SCISEARCH, LIFESCI, BIOSIS, EMBASE' ENTERED AT 11:35:38 ON 15 NOV 2005

L1 142 FILE MEDLINE
L2 124 FILE CAPLUS
L3 236 FILE SCISEARCH
L4 12 FILE LIFESCI
L5 119 FILE BIOSIS
L6 109 FILE EMBASE
TOTAL FOR ALL FILES
L7 742 S CYSTIC FIBROSIS AND INHIBITOR AND PROTEASE
L8 224 FILE MEDLINE
L9 214 FILE CAPLUS
L10 329 FILE SCISEARCH
L11 21 FILE LIFESCI
L12 185 FILE BIOSIS
L13 282 FILE EMBASE
TOTAL FOR ALL FILES
L14 1255 S CYSTIC FIBROSIS AND INHIBITOR AND (PROTEASE OR PROTEINASE)
L15 3 FILE MEDLINE
L16 6 FILE CAPLUS
L17 2 FILE SCISEARCH
L18 0 FILE LIFESCI
L19 4 FILE BIOSIS
L20 1 FILE EMBASE
TOTAL FOR ALL FILES
L21 16 S L14 AND KUNITZ
L22 11 DUP REM L21 (5 DUPLICATES REMOVED)

=> s l14 and trypsin inhibitor
L23 19 FILE MEDLINE
L24 18 FILE CAPLUS
L25 23 FILE SCISEARCH
L26 0 FILE LIFESCI
L27 16 FILE BIOSIS
L28 18 FILE EMBASE

TOTAL FOR ALL FILES
L29 94 L14 AND TRYPSIN INHIBITOR

=> s l29 not 1999-2005/py
L30 12 FILE MEDLINE
L31 5 FILE CAPLUS

```
L32          3 FILE SCISEARCH
L33          0 FILE LIFESCI
L34          9 FILE BIOSIS
L35         10 FILE EMBASE

TOTAL FOR ALL FILES
L36         39 L29 NOT 1999-2005/PY

=> dup rem l36
PROCESSING COMPLETED FOR L36
L37          23 DUP REM L36 (16 DUPLICATES REMOVED)

=> d ibib abs 1-23

L37  ANSWER 1 OF 23     MEDLINE on STN
ACCESSION NUMBER:    1998109096     MEDLINE Full-text
DOCUMENT NUMBER:     PubMed ID: 9447774
TITLE:               Alpha 1-antitrypsin deficiency: memorandum from a WHO
                     meeting.
AUTHOR:              Anonymous
SOURCE:              Bulletin of the World Health Organization, (1997) 75 (5)
                     397-415.  Ref: 81
                     Journal code: 7507052. ISSN: 0042-9686.
PUB. COUNTRY:        Switzerland
DOCUMENT TYPE:       (CLINICAL TRIAL)
                     Journal; Article; (JOURNAL ARTICLE)
                     General Review; (REVIEW)
                     (REVIEW, TUTORIAL)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199802
ENTRY DATE:          Entered STN: 19980306
                     Last Updated on STN: 20000303
                     Entered Medline: 19980223
AB      alpha 1-Antitrypsin (AAT) deficiency, also known as alpha 1-antiprotease inhibitor
        deficiency, is a disease caused by genetically determined AAT deficiency.  It occurs as a
        result of inheritance of two protease inhibitor (PI) deficiency alleles from the AAT gene
        locus (designated PI) on chromosomal segment 14q32.1.  The most common deficiency allele
        is PI*Z and a large majority of individuals with severe AAT deficiency are PI type ZZ.
        The disease occurs predominantly in white persons of European origin and its frequency in
        Europe and North America is comparable to that of cystic fibrosis (1 in 2000 to 1 in
        7000.) Persons with AAT deficiency may have no clinical manifestations.  Chronic
        obstructive pulmonary disease (COPD) with a high frequency of panacinar emphysema is the
        most prevalent clinical disorder associated with AAT deficiency and the most frequent
        cause of disability and death.  Tobacco smoking is the major risk factor for developing
        COPD, which generally begins by the third decade of life, much earlier than "usual" COPD
        that occurs in AAT-replete individuals.  Liver disease, the second most frequent clinical
        manifestation of AAT deficiency, typically presents as cholestasis in infancy but is
        usually not severe and generally remits by adolescence.  Chronic liver disease develops
        infrequently, although AAT deficiency is the commonest cause of chronic liver disease in
        childhood.  Cirrhosis and carcinoma of the liver affect at least 25% of AAT-deficient
        adults over the age of 50 years.  AAT deficiency appears to be widely underdiagnosed and
        based on predicted gene frequencies even in the most intensely studied populations, only a
        small proportion of those predicted to have AAT deficiency have been diagnosed.  Human AAT
        is available in limited quantity for augmentation therapy.  This Memorandum summarizes the
        discussions and recommendations made by participants at a WHO meeting held in Geneva on
        18-20 March 1996 to review existing knowledge about this highly prevalent genetic
        disorder, develop a strategy for enhancing awareness of it among health-care-givers and
        the general public, and explore new case-finding and disease-prevention strategies.


L37  ANSWER 2 OF 23  SCISEARCH  COPYRIGHT (c) 2005 The Thomson Corporation  on
     STN
ACCESSION NUMBER:    1997:244478  SCISEARCH Full-text
THE GENUINE ARTICLE: WP342
TITLE:               Purification, characterization, and localization of a
                     novel trypsin-like protease found in the human
                     airway
AUTHOR:              Yasuoka S (Reprint); Ohnishi T; Kawano S; Tsuchihashi S;
                     Ogawara M; Masuda K; Yamaoka K; Takahashi M; Sano T
CORPORATE SOURCE:    UNIV TOKUSHIMA, SCH MED SCI, DEPT NURSING, KURAMOTOCHO
```

3-18-15, TOKUSHIMA 770, JAPAN (Reprint); TEIJIN INST BIOMED RES, HINO, TOKYO 191, JAPAN; UNIV TOKUSHIMA, SCH MED, DEPT PATHOL 1, TOKUSHIMA 770, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY (MAR 1997) Vol. 16, No. 3, pp. 300-308.
ISSN: 1044-1549.
PUBLISHER: AMER LUNG ASSOC, 1740 BROADWAY, NEW YORK, NY 10019.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 37
ENTRY DATE: Entered STN: 1997
Last Updated on STN: 1997
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A novel trypsin-like protease was purified to homogeneity from the sputum of patients with chronic airway diseases, by sequential chromatographic procedures. The enzyme migrated on SDS-polyacrylamide gel electrophoresis to a position corresponding to a molecular weight of 28 kDa under both reducing and non-reducing conditions, and showed an apparent molecular weight of 27 kDa by gel filtration, indicating that it exists as a monomer. It had an NH2-terminal sequence of Ile-Leu-Gly-Gly-Thr-Glu-Ala-Glu-Glu-Gly-Ser-Trp-Pro-Trp-Gln-Val-Ser-Leu- Arg-Leu, which differed from that of any known protease. Studies with model peptide substrates showed that the enzyme preferentially cleaves the COOH-terminal side of arginine residues at the P1 position of certain peptides, cleaving Boc-Phe-Ser-Arg-4-methylcoumaryl- 7-amide most efficiently and having an optimum pH of 8.6 with this substrate. The enzyme was strongly inhibited by diisopropyl fluorophosphate, leupeptin, antipain, aprotinin, and soybean trypsin inhibitor, but hardly inhibited by secretory leukocyte protease inhibitor at 10 mu M. An immunohistochemical study indicated that the enzyme is located in the cells of the submucosal serous glands of the bronchi and trachea. These results suggest that the enzyme is secreted from submucosal serous glands onto the mucous membrane in patients with chronic airway diseases.

L37 ANSWER 3 OF 23 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:123590 SCISEARCH Full-text
THE GENUINE ARTICLE: WF992
TITLE: Inhibition of neutrophil elastase-induced interleukin-8 gene expression by urinary trypsin inhibitor in human bronchial epithelial cells
AUTHOR: Nakamura H (Reprint); Abe S; Shibata Y; Sata M; Kato S; Saito H; Hino T; Takahashi H; Tomoike H
CORPORATE SOURCE: YAMAGATA UNIV, SCH MED, DEPT INTERNAL MED 1, YAMAGATA 99023, JAPAN (Reprint)
COUNTRY OF AUTHOR: JAPAN
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (FEB 1997) Vol. 112, No. 2, pp. 157-162.
ISSN: 1018-2438.
PUBLISHER: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 40
ENTRY DATE: Entered STN: 1997
Last Updated on STN: 1997
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background: Urinary trypsin inhibitor (UTI), a potential inhibitor for proteinases including neutrophil elastase (NE), trypsin, plasmin, cathepsin B and H, has been used for the treatment of lung diseases with the absence of side effects in Japan. Methods: In this study, we investigated the inhibitory effects of UTI on both purified NE and NE activities present in bronchoalveolar fluids from patients with chronic bronchitis. We also investigated the inhibitory capacity of UTI with regard to NE-induced interleukin-X gene expression in human bronchial epithelial cells by Northern analyses. Results: UTI inhibited NE activities in bronchoalveolar lavage fluid from patients with chronic bronchitis and of the purified enzyme. In addition, UTI inhibited NE-induced interleukin-8 gene expression and protein secretion in a human bronchial epithelial cell line. Conclusions: Our results suggest that UTI is applicable to patients with a variety inflammatory lung diseases in which NE plays a pivotal role.

L37 ANSWER 4 OF 23 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 96034018 EMBASE Full-text
DOCUMENT NUMBER: 1996034018
TITLE: Inhibition of human pancreatic proteinases by mucus proteinase inhibitor, eglin c and aprotinin.
AUTHOR: Belorgey D.; Dirrig S.; Amouric M.; Figarella C.; Beith J.G.
CORPORATE SOURCE: Laboratorie d'Enzymologie, INSERM U392, Universita Louis Pasteur Strasbourg, F-67400 Ilkirch, France
SOURCE: Biochemical Journal, (1996) Vol. 313, No. 2, pp. 555-560.
ISSN: 0264-6021 CODEN: BIJOAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 960212
Last Updated on STN: 960212

AB The kinetic investigation of the inhibition of human pancreatic trypsin 1, trypsin 2 and chymotrypsin A by mucus proteinase inhibitor, eglin c and aprotinin reveals that (i) the first protein is a potent inhibitor of chymotrypsin A (k(ass.) = 1.4 x 106 M-1 s-1, K(i) = 71pM) but forms loose complexes with trypsin 1 (K(i) = 0.5 μM) and trypsin 2 (K(i) = 18 nM), (ii) eglin c does not inhibit the two trypsins but forms a tight complex with chymotrypsin A (k(ass.) = 3.3 x 106 M-1 s-1, K(i) < 0.1 nM) and (iii) aprotinin is a potent inhibitor of trypsin 1 (k(ass.) = 1 x 105 M-1 s-1, K(i) < 0.2 nM) and trypsin 2 (k(ass.) = 2.4 x 105 M-1 s-1, K(i) < 1 nM) but forms a loose complex with chymotrypsin A (K(i) = 0.17 μM). These data, together with those published previously on human pancreatic elastase, suggest that a cocktail of aprotinin + eglin c might be a better intensive-care drug for acute pancreatitis than aprotinin alone, because it will efficiently inhibit all four human pancreatic proteinases. On the other hand, human gastric juice inactivates mucus proteinase inhibitor by pepsin-mediated cleavage. This indicates that the fraction of mucus proteinase inhibitor that reaches the stomach following aerosol delivery to cystic fibrosis patients does not reach the duodenum in an active form and, therefore, does not aggravate the pancreatic insufficiency of these patients.

L37 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:453333 CAPLUS Full-text
DOCUMENT NUMBER: 125:141308
TITLE: Neutrophil elastase/α1-proteinase inhibitor complex levels decrease in plasma of cystic fibrosis patients during long-term oral β-carotene supplementation
AUTHOR(S): Winklhofer-Roob, Brigitte M.; Schlegel-Haueter, Susanna E.; Khoschsorur, Gholamali; Van't Hof, Martin A.; Suter, Susanne; Shmerling, David H.
CORPORATE SOURCE: Department Pediatrics, University Zurich, Switz.
SOURCE: Pediatric Research (1996), 40(1), 130-134
CODEN: PEREBL; ISSN: 0031-3998
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lung inflammation in cystic fibrosis (CF) is associated with an increased release from activated neutrophils of oxidants and proteinases. Free radical generation is not efficiently neutralized, and the major anti-proteinase, α1- proteinase inhibitor (α1-PI) is thought to be oxidatively inactivated. The authors hypothesized that enhanced antioxidant protection could represent an addnl. long-term strategy to attenuate the host inflammatory response. The effect on plasma neutrophil elastase/α1-PI (NE/α1-PI) complex levels (as a marker of lung inflammation) and plasma malondialdehyde concns. (as a marker of lipid peroxidn.) of addnl. oral β-carotene supplementation was studied in 33 CF patients who had already received long-term vitamin E supplementation. In the presence of a more than 10-fold increase in plasma β-carotene concns. (0.09 to 1.07 μmol/L), a small increase in plasma α-tocopherol concns. (23.8 to 28.4 μmol/L), and a more than 50%

decrease in plasma malondialdehyde concns. (1.00 to 0.46 μmol/L), plasma NE/α1-PI complex levels decreased from 102.2 to 83.0 μg/L;. Plasma retinol concns. increased (1.05 to 1.23 μmol/L) due to conversion of β-carotene to retinol, which could have contributed to the decrease in NE/α1-PI complex levels. Based on these results, the authors speculate that efficient antioxidant supplementation could attenuate lung inflammation in CF.

L37 ANSWER 6 OF 23 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:836686 SCISEARCH Full-text
THE GENUINE ARTICLE: TH982
TITLE: EFFECT OF NEUTROPHIL MEDIATORS ON EPITHELIAL PERMEABILITY
AUTHOR: PETERSON M W (Reprint); WALTER M E; NYGAARD S D
CORPORATE SOURCE: UNIV IOWA, DEPT INTERNAL MED, DIV PULM, IOWA CITY, IA 52242
COUNTRY OF AUTHOR: USA
SOURCE: AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY (DEC 1995) Vol. 13, No. 6, pp. 719-727.
ISSN: 1044-1549.
PUBLISHER: AMER LUNG ASSOC, 1740 BROADWAY, NEW YORK, NY 10019.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 55
ENTRY DATE: Entered STN: 1995
Last Updated on STN: 1995
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Inflammatory lung disease is associated with increased epithelial permeability, but it is unclear how inflammatory cells alter epithelial permeability. Neutrophils have azurophilic granules containing elastase, cathepsin G, and defensins which are released at sites of inflammation. Experiments using whole animals and cultured cells suggest that neutrophil elastase contributes to increased epithelial permeability. Using Madin-Darby canine kidney epithelial (MDCK) monolayers, a well-described epithelial model, we asked whether neutrophil elastase directly affects epithelial permeability independent of cell death or cell detachment from the substratum. We measured permeability using H-3-mannitol. We found that neutrophil elastase increased epithelial permeability in a time- and concentration-dependent fashion. Increased permeability required prolonged (greater than or equal to 6 h) exposure to elastase, but was not associated with cytolytic injury or cell detachment. These findings are potentially relevant to the lung because we found a similar time- and concentration-dependent effect when we added elastase to cultured human bronchial epithelial cells. In MDCK cells, permeability increased without alterations in cell actin at the light microscopic level. Interestingly, elastase-induced permeability was both prevented and reversed by serum, but not by serum albumin. Complete reversal occurred if serum was added up to 16 h after adding elastase. Proteolytic activity is important in HNE-induced epithelial permeability because soy bean trypsin inhibitor completely blocks the effect and alpha(1) proteinase inhibitor (alpha(1)PI) partially blocks the effect. Charge interactions also appear to be important because the polyanions heparin and sulfated dextran completely blocked increased permeability following elastase but only partially blocked elastolytic activity in isotonic solutions. In addition, other cationic neutrophil peptides, cathepsin G and defensins, acted cooperatively with elastase to increase permeability, These data provide direct evidence that neutrophil elastase alters normal epithelial barrier properties without killing the cells, and that elastase acts cooperatively with other soluble neutrophil mediators in causing target epithelial cell dysfunction. By altering epithelial permeability, elastase can contribute to the pathophysiology in many forms of inflammatory lung disease.

L37 ANSWER 7 OF 23 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 93089888 EMBASE Full-text
DOCUMENT NUMBER: 1993089888
TITLE: Consequences of unbalanced protease in the lung: Protease involvement in destruction and local defense mechanisms of the lung.
AUTHOR: Birrer P.
CORPORATE SOURCE: Department of Paediatrics, University of Berne, Inselspital,CH-3010 Bern, Switzerland

SOURCE: Agents and Actions, (1993) Vol. 40, No. SUPPL., pp. 3-12.
ISSN: 0065-4299 CODEN: AGACBH
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 930516
Last Updated on STN: 930516

AB Complex mechanisms regulate sequestration, retention and migration of neutrophils in the lung. Neutrophils can migrate into the lung without producing significant damage under some circumstances, whereas at other times great structural alteration occurs. A potential explanation lies in the phenomenon of priming, a state of altered responsivity of neutrophils. A wide variety of molecules are able to induce this higher degree of responsiveness including PAF, TNF, GM-CSF, and IL-1. Enhanced cellular responses include secretion, adhesion and synthetic function. Unprimed neutrophils can migrate through lung tissues, secreting but little of their contents, in the context of 'normal' inflammatory response. On the other hand neutrophils primed before the emigration phase, injury to the tissue they are migrating through would be likely by virtue of releasing toxic mediators. One of these mediators is neutrophil elastase, a potent protease. It is the purpose of this review to highlight the duality function of neutrophils as (i) one of the bodies highly effective host defense weapons and (ii) mediator of destruction and host defense impairment in the lung by releasing mediators such as neutrophil elastase.

L37 ANSWER 8 OF 23 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 89381949 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2476536
TITLE: Trypsin-binding immunoglobulin G and associated antigen in cystic fibrosis.
AUTHOR: Blandin C; Laroche D; Lemonnier F; Pasquet C; Travert G
CORPORATE SOURCE: Laboratoire de Biophysique medicale, CHU de Caen, France.
SOURCE: Journal of pediatric gastroenterology and nutrition, (1989 Jul) 9 (1) 13-6.
Journal code: 8211545. ISSN: 0277-2116.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19960129
Entered Medline: 19891025

AB Trypsin-binding immunoglobulin G (TBIgG) is found in the sera of a high proportion of patients with cystic fibrosis. We previously reported that TBIgG preferentially binds human cationic trypsin rather than trypsin from other animal species. Binding affinity is enhanced by complex formation with bovine pancreatic trypsin inhibitor, which is known to induce characteristic conformational modifications in the active site region of the trypsin molecule. To identify the human trypsin-like antigen associated with TBIgG, we have studied the effects of conformational changes of cationic trypsin induced by limited proteolysis based on competitive binding studies. It is shown that the most likely TBIgG-related self-antigen is an 11,000-dalton fragment that is a cleavage product of the complex formed by trypsin and alpha 1-protease inhibitor. This result emphasizes the occurrence of circulating trypsinogen activation and is interpreted to be a consequence of the protease-antiprotease imbalance, which has been well documented by previous investigators in cystic fibrosis and also in other lung diseases associated with an inflammatory state.

L37 ANSWER 9 OF 23 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 88136855 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2449319
TITLE: Protease inhibitor and defective proteolysis in cystic fibrosis.
AUTHOR: Hsieh M C; Berry H K
CORPORATE SOURCE: Children's Hospital Medical Center, Cincinnati, Ohio 45229.
SOURCE: Digestive diseases and sciences, (1988 Mar) 33 (3) 282-8.

Journal code: 7902782. ISSN: 0163-2116.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198803
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880331

AB Meconium specimens from 18 infants with cystic fibrosis (CF) had strong trypsin inhibitory activity (TIA). The same specimen, which contained increased quantities of undigested proteins, had normal concentrations of immunoreactive trypsin (IRT), but deficient trypsin catalytic activity (TCA). TIA was not detected in any specimen from non-CF infants who had high concentration of proteins comparable to that of CF infants. Subjecting meconium supernatant of CF infants to Sephadex G-75 gel filtration revealed that TCA was greatly enhanced in effluents after fractions were activated by porcine trypsin. TCA was present in the same fractions with IRT. The findings suggested that proteases were secreted into the intestinal lumen in CF infants prior to birth. Deficient proteolysis in the disease might be due to the presence of a trypsin inhibitor.

L37 ANSWER 10 OF 23 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 84132403 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6421611
TITLE: Sputum sol-phase proteins and elastase activity in patients with cystic fibrosis.
AUTHOR: Jackson A H; Hill S L; Afford S C; Stockley R A
SOURCE: European journal of respiratory diseases, (1984 Feb) 65 (2) 114-24.
Journal code: 8006891. ISSN: 0106-4339.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198404
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 20000303
Entered Medline: 19840412

AB Sputum and serum samples were obtained from 38 patients with cystic fibrosis seen as out-patients at routine follow-up, or from patients admitted with acute pulmonary exacerbations of their disease. Elastolytic activity was measurable in the sputum of 13 of 16 out-patient samples and detectable in 21 of 22 patients admitted with pulmonary exacerbation. The enzyme activity was inhibited by soy bean trypsin inhibitor and alpha 1 antitrypsin, but not by ethylenediamine tetracetic acid, suggesting that it was predominantly a serine proteinase, probably leucocyte elastase. The mean sputum/serum albumin ratio was 2.53 X 10(-2) (SD +/- 2.4) for the out-patients and this was not significantly different from those of patients admitted with pulmonary exacerbation. However, those patients admitted with fever had increased sputum/serum albumin ratios (mean = 4.66 X 10(-2); SD +/- 3.19) compared with those admitted with a normal temperature (mean = 1.52 X 10(-2); SD +/- 0.41. 2p less than 0.01). The albumin ratios of the pyrexial group fell with antibiotic therapy. The sputum/serum alpha 1 antitrypsin ratios were generally greater than expected (by comparison with albumin) and evidence is presented suggesting that this is due to immunological over-estimation.

L37 ANSWER 11 OF 23 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 82273808 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6180371
TITLE: Plasma arginine esterase in cystic fibrosis: kinetics of activation, identification as plasma kallikrein, reaction with alpha 2-macroglobulin and comparison with levels in normal plasma.
AUTHOR: Bury A F; Barrett A J
SOURCE: Pediatric research, (1982 Aug) 16 (8) 613-20.
Journal code: 0100714. ISSN: 0031-3998.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198210
ENTRY DATE: Entered STN: 19900317

Last Updated on STN: 20000303
Entered Medline: 19821029

AB Treatment of normal plasma with chloroform and ellagic acid yielded esterase activity against tosylarginine methyl ester, which reached a maximum within 2 h. After 2 h most or all of the activity as resistant to inhibition by soybean trypsin inhibitor (STI), but was still sensitive to the low molecular weight inhibitors di-isopropyl fluorophosphate, aprotinin and prolyl-phenylalanyl-arginyl chloromethane. The activity ran in gel chromatography with alpha 2 macroglobulin (ampha 2M), as if it were due to an alpha 2M proteinase complex. The generation of the arginine esterase activity by chloroform and ellagic acid was apparently dependent on the activation of factor XII, being blocked by Polybrene. In plasma pretreated with methylamine-HCl (an inactivator of alpha 2M), the arginine esterase was 95% sensitive to inhibition by STI. With regard to substrate specificity, inhibition characteristics, and gel chromatographic behaviour, it was indistinguishable from plasma kallikrein (EC 3.4.21.34, formerly 3.4.21.8). The chloroform and ellagic acid treatment of plasma resulted in a disappearance of prokallikrein simultaneous with the appearance of the arginine esterase. By these criteria, the arginine esterase activity was attributable entirely to plasma kallikrein either in its free form (methylamine-treated plasma) or bound to alpha 2M (buffer-treated plasma). Comparisons of STI-sensitive and STI-resistant arginine esterase activities of plasma samples from cystic fibrosis patients, obligate heterozyotes or other groups showed no significant differences in levels of activity, kinetics of activation or gel chromatographic behaviour. We conclude that cystic fibrosis is unrelated to any abnormality in plasma arginine esterase activity, contrary to some previous reports.

L37 ANSWER 12 OF 23 MEDLINE on STN
ACCESSION NUMBER: 82093827 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6172220
TITLE: Protease binding by alpha 2 macroglobulin in cystic fibrosis.
AUTHOR: Bridges M A; Applegarth D A; Johannson J; Wong L T; Davidson A G
SOURCE: Clinica chimica acta; international journal of clinical chemistry, (1982 Jan 5) 118 (1) 33-43.
Journal code: 1302422. ISSN: 0009-8981.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198203
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19970203
Entered Medline: 19820322

AB The interaction of alpha 2 macroglobulin (alpha 2M) with exogenous proteases has been reported by others to be abnormal in cystic fibrosis (CF). We have re-examined these claims. Four parameters were considered:(1) the molar protease binding of alpha 2M; (2) the interaction of bovine cationic trypsin (BCT), complexed to alpha 2M, with low molecular mass substrate, benzoyl arginine ethyl ester (BAEE); (3) the stability of formed alpha 2 M-BCT complexes; and (4) the subunit structure of alpha 2M. We have found CF alpha 2M to be similar to control alpha 2M in every respect studied.

L37 ANSWER 13 OF 23 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 80189385 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6990368
TITLE: Reaction of 4-methylumbelliferylguanidinobenzoate with proteases in human amniotic fluid.
AUTHOR: Walsh M M; Rao G J; Nadler H L
SOURCE: Pediatric research, (1980 Apr) 14 (4 Pt 1) 353-6.
Journal code: 0100714. ISSN: 0031-3998.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198007
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19800728

AB An arginine esterase activity similar to that observed in plasma has been demonstrated in second trimester and term human amniotic fluid. Like plasma, the protease(s) hydrolyzed esters of arginine, were reactive towards 4-methylumbelliferylguanidinobenzoate (MUGB), a

sensitive active site titrant of trypsin-like enzymes, and had a pI of 5.1--5.4. The pH optimum for proteolytic activity was 8.0. This protease activity was inhibited by soybean trypsin inhibitor (STI), benzamidine and (p-nitrophenyl)-p'-guanidinobenzoate (NPGB), and was insensitive to 1-chloro-3-tosylamido-7-amino-2-heptanone (TLCK) and p-hydroxymercuribenzoic acid (HMB). Upon gel filtration, two MUGB-reactive fractions were observed, one with an apparent molecular weight of 200,000 and the other, 100,000. Both fractions had arginine esterase activity and appeared to be sensitive to inhibition by STI and benzamidine. The mean MUGB titre value (nmoles of 4-methylumbelliferone released per ml amniotic fluid) for 300 mid-trimester amniotic fluids was 11.40 +/- 2.40 nmoles MU/ml. The mean specific activity was 2.36 +/- 0.41 nmoles MU/mg protein. Two amniotic fluids from pregnancies which delivered children with cystic fibrosis (CF) were analyzed in blind samples sent from other laboratories. The MU titre values obtained were 4.73 and 4.32 with specific activities of 1.24 and 1.30 respectively. A third was identified in our screening program of amniotic fluids obtained from amniocenteses done for the intrauterine detection of genetic abnormalities. The MU titre value was 5.52 nmoles/ml with a specific activity of 1.34. The specific activities of these fluids when compared to the controls were significantly different (p less than 0.001). The mean titre value for 23 term amniotic fluids samples was 8.14 +/- 1.69 nmoles MU/ml. The mean specific activity was 3.37 +/- 0.76 nmoles MU/mg protein. A term amniotic fluid obtained from a woman who delivered a baby with CF showed a markedly reduced level of MUGB reactivity (3.01 nmole/ml). The specific activity was 1.06 which was significantly different from the control term fluids. The MU titre values and specific activities of amniotic fluids obtained from abnormal pregnancies (such as those with neural tube defects, chromosomal abnormalities and polymorphisms, abortions and stillbirths) and fluids with elevated alphafetoprotein and maternal blood contaminants did not significantly vary from the mean control values (Table 3).

L37 ANSWER 14 OF 23 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 80107681 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6153257
TITLE: Trypsin binding activity of alpha 2-macroglobulin in cystic fibrosis and other lung diseases.
AUTHOR: Schidlow D V; Kueppers F
SOURCE: American review of respiratory disease, (1980 Jan) 121 (1) 31-7.
Journal code: 0370523. ISSN: 0003-0805.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198003
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19800317

AB Abnormalities of the interaction between alpha 2-macroglobulin and proteases have been suspected in cystic fibrosis . We measured the binding activity for trypsin of alpha 2-macroglobulin in 65 patients with cystic fibrosis, 41 obligate heterozygotes for cystic fibrosis, 18 children with asthma, 21 adult patients with chronic obstructive pulmonary disease, and 21 healthy control subjects. The assay was based on the observation that, once it is bound to alpha 2-macroglobulin, trypsin is no longer inhibited by soybean trypsin inhibitor. The bound trypsin retains activity against synthetic substrates such as N-alpha-benzoyl- arginine-p-nitroanilide. We found a moderately increased molar binding ratio of trypsin to alpha 2-macroglobulin in all patient groups and heterozygotes compared to healthy control subjects. The absolute concentration of alpha 1-macroglobulin was related to age rather than to the disease of the patient. Our data argue against a defect in protease-binding activity of alpha 2-macroglobulin in cystic fibrosis. The moderately increased binding activity observed could have been related to a structural difference in alpha 2-macroglobulin or to binding of ligands. This finding however, was not unique to patients with cystic fibrosis; the binding activity was increased in heterozygotes and in patients with other pulmonary diseases.

L37 ANSWER 15 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN .
ACCESSION NUMBER: 1980:77224 BIOSIS Full-text
DOCUMENT NUMBER: PREV198019014722; BR19:14722
TITLE: CYSTIC FIBROSIS EVIDENCE FOR CORRECTION OF ABNORMAL METABOLISM OF ANAPHYLATOXIN COMPLEMENT C-3A BY MONOCYTES MACROPHAGES IN-VITRO FOLLOWING ADDITION OF NORMAL ALPHA-2 MACRO GLOBULIN COMPLEXED WITH PROTEASES.

AUTHOR(S): WILSON G B [Reprint author]
CORPORATE SOURCE: DEP BASIC CLIN IMMUNOL MICROBIOL, MED UNIV SC, CHARLESTON, SC 29403, USA
SOURCE: Federation Proceedings, (1980) Vol. 39, No. 3, pp. ABSTRACT 967.
Meeting Info.: 64TH ANNUAL MEETING OF THE FED. AM. SOC. EXP. BIOL., ANAHEIM, CALIF., USA, APR. 13-18, 1980. FED PROC.
CODEN: FEPRA7. ISSN: 0014-9446.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH

L37 ANSWER 16 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1980:175638 BIOSIS Full-text
DOCUMENT NUMBER: PREV198069050634; BA69:50634
TITLE: ANOMALOUS ALPHA-2 MACRO GLOBULIN PROTEASE COMPLEXES IN CYSTIC FIBROSIS DECREASED UPTAKE OF THE COMPLEXES BY FIBROBLASTS IN CULTURE.
AUTHOR(S): VAN LEUVEN F [Reprint author]; CASSIMAN J J; VAN DEN BERGHE H
CORPORATE SOURCE: DIV HUM GENET, DEP HUM BIOL, UNIV LEUVEN, LEUVEN, BELG
SOURCE: Pediatric Research, (1979) Vol. 13, No. 12, pp. 1384-1385.
CODEN: PEREBL. ISSN: 0031-3998.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Immunochemical and functional properties of control and cystic fibrosis (CF) α2-macroglobulin (α2M) are compared. Crossed immunoelectrophoresis and Ouchterlony double diffusion revealed no qualitative differences between the 2 α2M-preparations. Trypsin-esterase activity assayed with BAPNA [benzoyl-arginyl-p- nitroanilide] as a substrate, in the presence of excess STI [soybean trypsin inhibitor], gave similar ratios between total and active α2M. These α2M-trypsin complexes were equally stable under various experimental conditions and maintained a constant STI non-inhibited esterase activity. Normal and CF-α2M-trypsin complexes were taken up by normal human fibroblasts to a similar extent during a 4 h period. The only significant difference was observed when the uptake of α2M from untreated sera was examined. The uptake of α2M from CF sera was always lower than from pooled control sera despite large variation. Mixing of control and CF serum did not affect the normal uptake and other serum components were taken up to the normal extent. Intracellular degradation of CF α2M had a half life of 2.0-2.8 h, which compares well to the normal half life of 2.2 h. More work needs to be done on the nature of the interaction between α2M and proteases before a reasonable explanation for the molecular nature of the abnormal behavior can be sought. This in vitro system may be of value for the study of the molecular anomaly in the α2M- protease complex of patients with CF. These observations may represent a rapid, quantitative and reproducible assay for the detection of patients with CF. Optimalization of the assay might allow detection of heterozygotes and could result in prenatal diagnosis of CF using amniotic fluid samples. Applicability of this study to genetic counseling is implied.

L37 ANSWER 17 OF 23 MEDLINE on STN
ACCESSION NUMBER: 80024183 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 488055
TITLE: Protease deficiency in plasma of patients with cystic fibrosis. Reduced reaction of 4-methylumbelliferylguanidinobenzoate with plasma of patients with cystic fibrosis.
AUTHOR: Walsh-Platt M; Rao G J; Nadler H L
SOURCE: Enzyme, (1979) 24 (4) 224-9.
Journal code: 1262265. ISSN: 0013-9432.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197912
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19791227

AB Protease activity in plasma is assayed using 4-methylumbelliferylguanidinobenzoate. The assay is modified by carrying out the reaction in the presence and absence of benzamidine, a competitive inhibitor of trypsin-like proteases. The parameters of the assay are described in detail. Using this assay, our earlier demonstration of a deficiency of protease activity in plasma of patients with cystic fibrosis is confirmed. The activity, corrected for the nonspecific hydrolysis of 4- methylumbelliferylguanidinobenzoate by benzamidine, is expressed as nanomoles of 4-methylumbelliferone released per milliliter plasma. Under standard conditions, the activity in plasma activated with chloroform-ellagic acid was 127.2 +/- 23.1 in 7 controls, 70.4 +/- 11.7 in 11 obligate heterozygotes, and 48.7 +/- 16.6 in 12 patients with cystic fibrosis. Identical results were obtained when unactivated plasma was used. These data demonstrate that the judicious use of specific inhibitors such as benzamidine might be useful in assaying low levels of protease activity in crude systems.

L37 ANSWER 18 OF 23 MEDLINE on STN
ACCESSION NUMBER: 79164528 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 312055
TITLE: Screening for cystic fibrosis in the newborn by meconium analysis.
AUTHOR: Ryley H C; Neale L M; Brogan T D; Bray P T
SOURCE: Archives of disease in childhood, (1979 Feb) 54 (2) 92-7. Journal code: 0372434. ISSN: 1468-2044.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197906
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19790611

AB During a 4-year routine screening programme for cystic fibrosis (CF) 15 464 specimens were examined for raised meconium albumin levels by a test strip method and by electroimmunoassay. The incidence of false-positive results was about 5 per 1000 specimens in either test. This could be reduced by 90% by determining the ratio of albumin : alpha-1-trypsin inhibitor (a ratio below 2.0 being considered as a negative result), and it could be reduced to zero by determining the ratio in subsequent faecal specimens. Three of 12 meconium specimens from infants with proved CF gave false-negative results in all 3 tests. The other 9 specimens had greater than 100 mg albumin/g dry weight and albumin: alpha-1-trypsin inhibitor ratios of greater than 3.0; in subsequent faecal specimens the ratios were over 4.0. 176 meconium specimens from elsewhere in the UK were examined and these included 23 from infants who were subsequently proved to have CF. Six of these 23 CF specimens gave false-negative results, the other 17 being strongly positive. The origins of meconium serum protein suggest that infants with CF in whom meconium gives false-negative results have normal pancreatic functions at birth. The specificity of current meconium tests therefore cannot be improved as they depend on pancreatic dysfunction.

L37 ANSWER 19 OF 23 EMBASE
ACCESSION NUMBER: 77211836 EMBASE Full-text
DOCUMENT NUMBER: 1977211836
TITLE: [Genetics and chronic obstructive bronchopneumopathies]. GENETIQUE ET BRONCHOPNEUMOPATHIES CHRONIQUES OBSTRUCTIVES. ASPECTS ACTUELS.
AUTHOR: Dyan A.; Bignon J.
CORPORATE SOURCE: Hop. Laennec, Paris, France
SOURCE: Concours Medical, (1976) Vol. 98, No. 46, pp. 7373-7383. CODEN: COMEAO
DOCUMENT TYPE: Journal
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
007 Pediatrics and Pediatric Surgery
LANGUAGE: French

AB At the present time only a few factors are known that are directly responsible for, or predispose to emphysema and to obstructive chronic bronchopneumopathies. Mucoviscidosis is an exceptional genetic factor, at least in the adult. The complete form is observed in the child, combining pancreatic insufficiency and severe bronchopathy. In the young adult mucoviscidosis comes up for discussion only very exceptionally in isolated bronchitic forms. Deficiency of alpha 1 antitrypsin is another genetic factor and is more important

in the adult than in the child; its linkage with pulmonary emphysema and the obstructive chronic bronchopneumopathies is described. This deficiency is of hereditary transmission, and a complex protein system (protease inhibitor system Pi) has been demonstrated. There is no doubt that these genetic factors are not the only causes. They certainly come into action in association with environmental factors (tobacco, pollution, bronchial infections and allergens). The practitioner is nowadays better armed for the struggle against these environmental factors, but study of the genetic factors predisposing to obstructive chronic bronchopneumopathies is a much more promising line of research in this wide sector of pneumology than are chronic bronchitis and pulmonary emphysema.

L37 ANSWER 20 OF 23 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 76268606 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 60735
TITLE: Absence of an alpha two-macroglobulin-protease complex in cystic fibrosis.
AUTHOR: Shapira E; Rao G J; Wessel H U; Nadler N L
SOURCE: Pediatric research, (1976 Sep) 10 (9) 812-7.
Journal code: 0100714. ISSN: 0031-3998.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197610
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19761020

AB The present study using immunologic methodology confirms previous observations from this laboratory of an absence of a protease component with arginine esterase activity in plasma of patients with cystic fibrosis. In this study, the pooled plasma from control individuals was activated and partially purified after adsorption on columns of soybean trypsin inhibitor conjugated to Sepharose 4B followed by elution with benzamidine. The fraction was further purified by isoelectrofocusing on polyacrylamide gels. Proteins around the pI range of 5.5 were eluted and utilized to prepare an antiserum. Immunoelectrophoresis of activated plasma samples from control subjects and patients with cystic fibrosis was performed utilizing the antiserum. In controls, four precipitin arcs with residual esterase activity were observed, whereas only three were seen in plasma from patients with cystic fibrosis. Double gel diffusion experiments using specific antisera ruled out the presence of trypsin, chymotrypsin, plasminogen, prothrombin, C1 esterase, alpha one- trypsin inhibitor, and inter-alpha-trypsin inhibitor in the concentrated benzamidine eluate. The antisera to alpha two-macroglobulin gave an immunoprecipitate which was readily stained for proteolytic activity. On immunoelectrophoresis, the alpha two-macroglobulin precipitin band corresponded to the band absent in plasma of patients with cystic fibrosis. In contrast, the alpha two-macroglobulin levels were similar in plasma of control subjects and patients with cystic fibrosis. Using the antiserum to the protein fractith proteolytic activity could be demonstrated in control plasma. One specific enzyme-active "rocket" was absent in plasma of patients with cystic fibrosis. In a double blind study of 15 control samples and 15 samples from patients with cystic fibrosis, a specific "rocket" was shown to be present in 13 control samples and absent in 14 cystic fibrosis samples. alpha two-Macroglobulin was determined by both an immunologic procedure and by its trypsin binding (trypsin protein esterase concentration). The ratio of the immunologic assay to the biologic activity assay was 90 for the normal plasma samples and only 65 for cystic fibrosis samples.

L37 ANSWER 21 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1976:12504 BIOSIS Full-text
DOCUMENT NUMBER: PREV197612012504; BR12:12504
TITLE: DEFICIENCY OF PROTEASE ACTIVITY IN PLASMA OF PATIENTS WITH CYSTIC FIBROSIS.
AUTHOR(S): RAO G J S; NADLER H L
SOURCE: Journal of Pediatrics, (1975) Vol. 86, No. 6, pp. 978-979.
CODEN: JOPDAB. ISSN: 0022-3476.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: Unavailable

L37 ANSWER 22 OF 23 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 76153487 EMBASE Full-text

DOCUMENT NUMBER: 1976153487
TITLE: Screening for cystic fibrosis by analysis of meconium for albumin and protease inhibitors.
AUTHOR: Ryley H.C.; Neale L.M.; Brogan T.D.; Bray P.T.
CORPORATE SOURCE: Dept. Med. Microbiol., Welsh Nat. Sch. Med., Univ. Hosp. Wales, Cardiff, United Kingdom
SOURCE: Clinica Chimica Acta, (1975) Vol. 64, No. 2, pp. 117-125.
CODEN: CCATAR
DOCUMENT TYPE: Journal
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
029 Clinical Biochemistry
048 Gastroenterology
LANGUAGE: English

AB A qualitative method of detecting elevated meconium protein concentration was compared with a method of determining meconium albumin concentration by electroimmunoassay since elevated meconium protein levels can indicate pancreatic insufficiency caused by cystic fibrosis. Between 5 and 10 per 1000 healthy infants passed meconium specimens that gave a false positive reaction with the Boehringer Mannheim test strip and contained a greater than expected concentration of albumin. It was possible to exclude pancreatic insufficiency in all of these children by determining the ratio, albumin : α1 antitrypsin in meconium and subsequent faecal specimens, since it was found that values of this ratio in excess of 2.0 suggested pancreatic insufficiency of the type associated with cystic fibrosis. Three of 14 neonates with subsequently proven cystic fibrosis yielded meconium specimens giving negative test strip results and low albumin concentrations. In two of these patients, the ratio, albumin : α1 antitrypsin in the meconium was within normal limits but, within two months of birth, the albumin : α1 antitrypsin ratio in the faeces of both children was greater than 3.0 suggesting that pancreatic insufficiency had developed.

L37 ANSWER 23 OF 23 MEDLINE on STN
ACCESSION NUMBER: 68011492 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6052961
TITLE: Inhibition of protease activity in purulent sputum by DNA.
AUTHOR: Lieberman J
SOURCE: Journal of laboratory and clinical medicine, (1967 Oct) 70 (4) 595-605.
Journal code: 0375375. ISSN: 0022-2143.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 196712
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19900101
Entered Medline: 19671218

=> log y